Antibiotic resistance among *Neisseria meningitidis* isolates in England, Wales and Northern Ireland (July 2010 - August 2019)

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Master of Science (by Research) 2021

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Abbreviations

3GC	Third generation cephalosporin(s)
AA	Amino acid(s)
AAS	Amino acid substitution(s)
ABR	Antibiotic resistance
AST	Antibiotic susceptibility testing
bp	Base pair(s)
CBA	Columbian blood agar
CC	Clonal complex(es)
CLSI	Clinical Laboratory Standards Institute
CPS	Capsular polysaccharide
CSF	Cerebral spinal fluid
EUCAST	European Committee on Antimicrobial Susceptibly Testing
DUS	DNA uptake sequence
E, W and NI	England, Wales and Northern Ireland
fHbp	Factor H binding protein
HGT	Horizontal gene transfer
IMD	Invasive meningococcal disease
KSA	Kingdom of Saudi Arabia
Mabs	Monoclonal antibodies
MAC	Membrane attack complex
MenA/B/C/NG/W/Y	Meningococcal serogroup A/B/C/NG/W/Y
MGL	Meningococcal genome library
MIC	Minimum inhibitory concentration(s)
MLST	Multi-locus sequence typing
MRU	Meningococcal Reference Unit
NadA	Neisserial adhesin A
NHBA	Neisseria Heparin Binding Antigen
NG	Non-groupable
NT	Non-typeable/subtypable
OMP	Outer membrane protein(s)
PBP	Penicillin binding protein
PenI	Penicillin-susceptible, increased exposure
PenR	Penicillin-resistant
PenS	Penicillin-susceptible, standard exposure
PorA	Porin A
PorB	Porin B
PHE	Public Health England
RT	Room temperature
ST	Sequence type(s)
VR	Variable region(s)
WGS	Whole genome sequencing
WT	Wild type

Abstract

Invasive meningococcal disease (IMD), caused by *Neisseria meningitidis*, has a fatality rate as high as 10%, even with appropriate treatment. In the UK, penicillin is administered to patients in primary care whilst cefotaxime and ceftriaxone are administered in secondary care. The first-choice antibiotic for chemoprophylaxis of close contacts is ciprofloxacin, followed by rifampicin. IMD caused by non-groupable (NG) meningococci affects mainly immunocompromised individuals, who are recommended antibiotic chemoprophylaxis due to a greater risk of IMD development.

Resistance to antibiotics among meningococci is relatively rare, however reduced susceptibility and resistance to penicillin is increasing globally. Limited data exist regarding the prevalence of antibiotic resistance among meningococci in the UK.

The Public Health England Meningococcal Reference Unit receives all isolates from IMD cases in England, Wales and Northern Ireland. The aims of this project were to i) investigate the distribution of antibiotic resistance to penicillin, rifampicin, ciprofloxacin and cefotaxime among IMD isolates from 2010/11-2018/19 (n=4,122), ii) investigate a recent outbreak of IMD in England caused by a ciprofloxacin-resistant NG meningococcal strain and iii) investigate increasing levels of penicillin resistance among serogroup W ST-11 clonal complex isolates in England.

Out of the 4,122 IMD isolates, 113 were penicillin-resistant, two were rifampicin-resistant, five were ciprofloxacin-resistant and one was cefotaxime-resistant. Penicillin resistance was mainly due to altered *penA* alleles. Rifampicin and ciprofloxacin resistance were due to altered *rpoB* and *gyrA* alleles, respectively. Cefotaxime resistance was observed in an isolate with an altered *penA* allele containing additional mutations to those harboured by penicillin-resistant isolates.

A ciprofloxacin-resistant strain of the ST-175 CC with an apparent propensity for reduced susceptibility to penicillin was identified and found to be of concern among immunocompromised individuals. An increase in penicillin-resistant English serogroup W

ST-11 CC isolates was due to several strains; in particular, a strain first identified in Australia in 2016. This research highlights the need for continued surveillance of antibiotic resistance among meningococci and the need for vigilance among immunocompromised patients to maintain successful chemoprophylaxis regimes.

1 Introduction

1.1 *Neisseria meningitidis*

The bacterium *Neisseria (N). meningitidis*, (the meningococcus), is an exclusively human commensal/pathogen colonising the nasopharynx of approximately 10% of people (Caugant and Maiden, 2009). Rarely the bacteria cross the endothelium causing invasive disease. The genus *Neisseria* also includes *N. gonorrhoeae*, causing the sexually transmitted disease gonorrhoea, along with several other non-pathogenic commensals (Liu et al., 2015).

1.1.1 Meningococcal carriage

Carriage is the main source of meningococcal transmission, occurring through respiratory secretions via person-to-person contact (Yazdankhah and Caugant, 2004). Carriage rates vary among different age groups, with relatively low rates among infants, which increase gradually, peaking at around 25% in adolescents and young adults (Christensen et al., 2010). Carriage risk factors include social behaviours and confinement to closed/semi-closed populations, e.g. pilgrims, university students and military personnel, where close contact and therefore transmission increases (Peterson et al., 2018). Carriage is a prerequisite for invasive meningococcal disease (IMD).

1.1.2 Invasive meningococcal disease

IMD was first reported in the early 19th century following an outbreak in Geneva, Switzerland (Vieusseux, 1805). It occurs when colonised meningococci cross the epithelial barrier of the nasopharynx into the bloodstream, and from here, may cause sepsis. If meningococci cross the blood brain barrier, gaining entry to the cerebral spinal fluid (CSF), they may cause meningitis (Coureuil et al., 2012). Other sites that can be affected alone or

in combination include joints, the pericardium and inner eye (Morgan et al., 2002; Joyce et al., 2003; Orden et al., 2003).

IMD, manifesting in meningitis and/or sepsis, is a life-threatening illness. Even with early diagnosis and treatment, IMD is associated with a mortality rate of around 5-10%; considerably lower than if left untreated (Brouwer et al., 2010; Castillo et al., 2011). Survivors may face long-term sequelae, such as limb amputations and sensorineural hearing loss (Pace and Pollard, 2012).

1.1.2.1 Clinical manifestations

IMD may present in various manifestations ranging in severity, including transient meningococcaemia, septic shock, multiple organ failure and death (Brandtzaeg et al., 1989). Meningitis is the most common presentation of IMD, occurring in around 40% of IMD cases (European Centre for Diseases Prevention and Control, 2013). Symptoms include fever, headache, neck stiffness, nausea and vomiting. Children <2 years may lack typical symptoms, presenting mainly with irritability, lethargy and occasionally, raised fontanelles (Riordan et al., 1995; Hart and Thomson, 2006).

Sepsis, which may lead to septic shock, circulatory and organ failure, presents as the main manifestation of IMD in around 30% of cases (Cai et al., 2010). It may also present in conjunction with meningitis (European Centre for Diseases Prevention and Control, 2013). Symptoms during the early stages of septicaemia include leg pain, cold peripheries and a non-blanching rash, which if left untreated causes skin discolouration and necrosis (Thompson et al., 2006; Pace and Pollard, 2012). Subsequent skin grafts, and in severe cases limb amputations, are just some of the complications that 10-20% of IMD survivors may face (Olbrich et al., 2018). Other sequelae include hearing loss and neurological impairment.

Uncommon manifestations of IMD, occurring in less than 10% of cases, include conjunctivitis and arthritis (European Centre for Diseases Prevention and Control, 2013).

1.1.2.2 Laboratory diagnosis and treatment

Hospital admission is a priority when IMD is suspected (Public Health England, 2012). In the UK, patients in primary care with suspected meningococcal disease are administered a single dose of benzylpenicillin (National Institute for Health and Care Excellence, 2015). Third generation cephalosporins (3GCs), ceftriaxone and cefotaxime, are administered following hospital admission and confirmation of IMD.

Confirmation of IMD is achieved by obtaining a culture of the organism or by detection of meningococcal DNA in a usually sterile site.

1.1.2.2.1 Meningococcal Reference Unit

In England, Wales and Scotland, identification of meningococci requires notification to Public Health England (PHE). Voluntary notification to the Public Health Agency is applied in Northern Ireland. The PHE Meningococcal Reference Unit (MRU) offers a free national reference service for confirmation and characterisation of meningococcal isolates in England, Wales and Northern Ireland (E, W and NI).

Culture remains the gold standard for IMD diagnosis, however early administration of antibiotics often prevents culture obtainment. The meningococcal PCR screening assay for clinical specimens targets the meningococcal capsular gene, *ctrA*, and has led to improved IMD confirmation since its implementation into the MRU service in 1996 (Hackett et al., 2002; Gray et al., 2006). Around 50% of IMD cases in E, W and NI are confirmed solely by PCR (Heinsbroek et al., 2013).

The screening PCR and associated PCR assays also serve to characterise the meningococcal capsular group (section 1.3.1.1). All cultured isolates undergo capsular serogrouping and serotyping and serosubtyping for the outer membrane proteins Porin B (PorB) and Porin A (PorA), respectively. They also undergo antibiotic susceptibility testing (AST) (section 1.3.1.5) and since July 2010, have undergone whole genome sequencing (WGS) (section 1.3.1.4).

1.1.3 Cell surface features

1.1.3.1 Capsule

The capsule is the main virulence factor of meningococci with its anti-phagocytic properties essential for survival and growth in the bloodstream of healthy individuals. An increased resistance to cationic antimicrobial peptides, which are essential components of the host innate defence system, is the likely protective mechanism of the meningococcal capsule (Spinosa et al., 2007). Almost all meningococcal isolates recovered from non-immunocompromised individuals are encapsulated, with unencapsulated meningococci very rarely the cause of IMD (McNamara et al., 2016; Santos-Neto et al., 2019). The polysaccharide capsule composition of meningococci forms the basis for the species' main classification system: grouping (section 1.3.1.1).

1.1.3.2 Outer membrane proteins

The outer membrane of meningococci contains various outer membrane proteins (OMPs), including porins (porin A and porin B), opacity associated proteins and surface adhesins (type IV pili). Many contribute to the organisms' pathogenicity by aiding in adhesion and invasion of epithelial cells as well as in the evasion of complement mediated killing (Table 1-1).

Table 1-1: Outer membrane components of meningococci.

Outer Membrane Component	Function	Reference
Porin A (PorA)/ Porin B (PorB)	- Enables diffusion of hydrophilic molecules in and out of cell - Provides characterisation due to variation between strains - Forms basis of typing/subtyping (section 1.3.1.2) - Vaccine antigen (porA)	(Jeanteur et al., 1991) (Jolley et al., 2007) (Jodar et al., 2002; Serruto et al., 2012).

Opacity associated proteins	- Mediates interaction between host - Facilitates adhesion and colonisation in the nasopharynx	(Virji et al., 1993) (De Jonge et al., 2002)
Type IV pili	- Facilitates initial contact of encapsulated meningococci - Aids in attachment to epithelial cells in nasopharynx -Has a role in DNA uptake for transformation - Has a role in motility	(Nassif et al., 1997) (Cehovin et al., 2013) (Eriksson et al., 2015)
Factor H binding protein (fHbp)	- Binds factor H promoting evasion of complement mediated killing - Vaccine antigen (section 1.2.2)	(Madico et al., 2006)
Neisserial adhesin A (NadA)	- Aids in adhesion to epithelial cells and subsequent invasion - Vaccine antigen (section 1.2.2)	(Capecchi et al., 2005)
Neisseria Heparin Binding Antigen (NHBA)	- Binds heparin promoting evasion of complement mediated killing - Vaccine antigen (section 1.2.2)	(Vacca et al., 2016)

1.1.4 The meningococcal genome

The meningococcal genome consists of a single circular chromosome of ~2.2 million base pairs (bp) (Parkhill et al., 2000; Tettelin et al., 2000). It contains a high proportion of repeated DNA sequences, including the 10-12 bp DNA uptake sequence (DUS) (Goodman and Scocca, 1988; Ambur et al., 2007). DUS is essential for uptake of exogenous DNA via horizontal gene transfer (HGT) by transformation, and integration into the chromosome by homologous recombination (Bäckman et al., 2000). Transformation allows for exchange of antibiotic resistance-associated genes between both the same and different species (Spratt et al., 1992; Alfsnes et al., 2018). The large number of DUSs and the natural competence of *N. meningitidis* make it readily available for DNA uptake, and co-colonisation with commensal *Neisseria* species in the nasopharynx makes transformation and recombination the main source of new genetic information and the main mechanism for the spread of antibiotic resistant-associated genes (Caugant and Brynildsrud, 2020). Plasmids exchanged through conjugation may also confer antibiotic resistance (ABR) (Roberts, 1989; Bäckman et al., 2000).

1.2 Prevention of invasive meningococcal disease

1.2.1 Immunity

Transfer of maternal antibodies offers protection against IMD during the first six months of life, after which IMD incidence increases (Goldschneider et al., 1969a). Naturally acquired immunity, a result of carriage acquisition, leads to a decrease in IMD incidence from around two years of age (Goldschneider et al., 1969b). Circulating serum bactericidal antibodies against meningococci act as opsonins, targeting cells for phagocytosis and activating the complement system (Kvalsvig and Unsworth, 2003).

The complement system, inducing phagocytosis and cell lysis, is vital for IMD prevention. The complement system is activated by three pathways: the classical, alternative and lectin pathways. Both alternative and lectin pathways form part of the innate immune response, directly activated by components on the pathogens surface. The classical pathway is antibody mediated, an effector of the adaptive immune response. All three pathways lead to cleavage of the complement protein, C3 (Lewis and Ram, 2014). C3b is produced, acting as an opsonin to promote phagocytosis of invading meningococcal cells (Ehlenberger and Nussenzweig, 1977). It is also used in the formation of C5 convertase, which cleaves C5 initiating the terminal complement pathway and formation of the Membrane Attack Complex (MAC). A multiprotein structure consisting of C5b-9, the MAC imbeds into the meningococcal cell membrane forming a pore and causing cell lysis (Schneider et al., 2007).

1.2.2 Vaccination

First licenced in the 1970s, meningococcal capsular polysaccharide (CPS) vaccines proved successful in controlling epidemics worldwide (Gold and Artenstein, 1971; Wahdan et al., 1973; Peltola et al., 1977). Plain meningococcal polysaccharides are limited by their low and short-lived immunity in young children (Gold et al., 1975, 1979). Thus, these were superseded by CPS-conjugate vaccines eliciting stronger, longer-lived immune responses, including in infants, the initiation of immune memory and the reduction of carriage

acquisition (Baraldo et al., 2005; Khatami et al., 2011; Terranella et al., 2011; Baxter et al., 2016). Implementation of these into the UK routine immunisation schedule (Table 1-2) have been crucial in controlling IMD, particularly IMD caused by meningococcal serogroups C (MenC) and W (MenW).

Table 1-2: Vaccines in the UK routine immunisation schedule for meningococcal serogroups A, C, W and Y.

Vaccine	Year	Details
MenC CPS-conjugate vaccine	1999 - 2006	- In response to UK increase in MenC disease during the 1990s (Wise, 1999). - Overall reduction of 86.7% in targeted age group (<20 years) (Balmer et al., 2002). - Removed from UK immunisation schedule in 2006 due to low MenC disease and protection from herd immunity.
MenC/Hib conjugate vaccine	2006 – Present	- Combined Hib (Haemophilus influenzae type b) and MenC vaccine for babies >1 year.
MenACWY quadrivalent CPS-conjugate	2015 - Present	- In response to UK increase in MenW disease from 2009 (Campbell et al., 2017). -Replaced MenC vaccine in 13-14-year olds and offered to new university students ≤25 years. - 69% reduction in MenW cases compared with predicted cases (Campbell et al., 2017).

CPS vaccines have proved unsuccessful against serogroup B meningococcal (MenB) disease due to a lack of immunogenicity of the MenB capsule (Finne et al., 1983). Vaccine approaches against serogroup B strains have therefore focused on the use of outer membrane vesicles (OMVs) and sub-capsular proteins of meningococci. OMV vaccines have been successful during outbreaks of MenB resulting from a single strain with a particular porA (Bjune et al., 1991; Arnold et al., 2011), however their use can be limited due to poor cross reactivity against diverse strains. Two MenB vaccines (Table 1-3) are currently licenced in the UK and elsewhere (Rivero-Calle et al., 2019); 4CMenB (Bexsero), which contains sub-capsular proteins combined with OMVs derived from the meningococcal outbreak strain of New Zealand (NZ98/254 strain) (Martin et al., 1998; Serruto et al., 2012)

and MenB-fHbp (Trumenba) (Perez et al., 2018). The UK was the first country to implement 4CMenB into the UK routine immunisation schedule in 2015. Over the first three years, vaccine effectiveness in England was 59% in infants receiving two doses and a booster, rising to 71.2% when considering only vaccine-preventable MenB isolates (Ladhani et al., 2020).

Peptides, and their antigenic cross reactivity, can vary. Owing to the diversity of peptide antigens among meningococci and differences in surface expression levels, MenB vaccines do not offer protection against all MenB strains. This has led to the development of several phenotypic predictors of coverage, including ELISA-based meningococcal antigens typing system (MATS; Bexsero) and flow cytometry-based meningococcal antigen surface expression (MEASURE; Trumenba) assay. There are also genotypic methods including MATS-based genotypic (g)MATS for Bexsero and the meningococcal deduced vaccine antigen reactivity (MenDeVAR) based on MATS (Bexsero) and MEASURE/hSBA (Trumenba).

Sub-capsular antigens may cause immune responses against meningococci irrespective of serogroups and therefore potentially against unencapsulated meningococci (Mulhall et al., 2018).

Table 1-3: Components of meningococcal serogroup B vaccines licensed for use in the UK.

Vaccine	Antigens	Cross reacts with
4CMenB (Bexsero®)	NadA peptide 8 (variant NadA2/3)	NadA-1 and NadA-2/3 peptides (Serruto et al., 2012).
	fHbp peptide 1 (nonlipidated variant 1)	fHbp variant 1 peptides (Serruto et al., 2012).
	NHBA peptide 2	Cross-reactive variant groups not defined.
	Outer membrane vesicles containing PorA subtype P1.4 (from the NZ98/254 strain used in the MenZB® vaccine)	PorA P1.4.

MenB-fHbp (Trumenba)	fHbp peptide 55 (lipidated variant 1)	fHbp Variant 1 peptides (Jiang et al., 2010).
	fHbp peptide 45 (lipidated variant 3)	fHbp variant 2 and 3 peptides (Jiang et al., 2010).

1.2.3 Chemoprophylaxis

To eliminate carriage and onward transmission/secondary cases, antibiotic chemoprophylaxis is offered to IMD cases where intravenous 3GCs were not used in treatment and offered to close contacts of cases. In the UK, ciprofloxacin is the antibiotic of choice, followed by rifampicin (Public Health England, 2012). Ongoing chemoprophylaxis is recommended for individuals with deficiencies of the terminal complement pathway, where IMD development risk is 1,000-10,000-fold higher than in those with functioning complement systems (Hellenbrand et al., 2015), and recurrent infection is prevalent (Figueroa et al., 1993).

1.3 Surveillance and epidemiology of invasive meningococcal disease

National surveillance of IMD is essential for identifying emerging hyper-virulent strains and during cluster/outbreak periods. It's essential for monitoring epidemiology to guide public health management, vaccination strategies and surveillance of ABR (Brehony et al., 2007).

1.3.1 Classification/characterisation of meningococcal strains

Historically, meningococcal strains have been characterised by phenotypic methods to determine the capsular group, PorB serotype and PorA serosubtype. Developments of genotypic methods have enabled characterisation at higher resolution, revolutionising epidemiological monitoring of IMD.

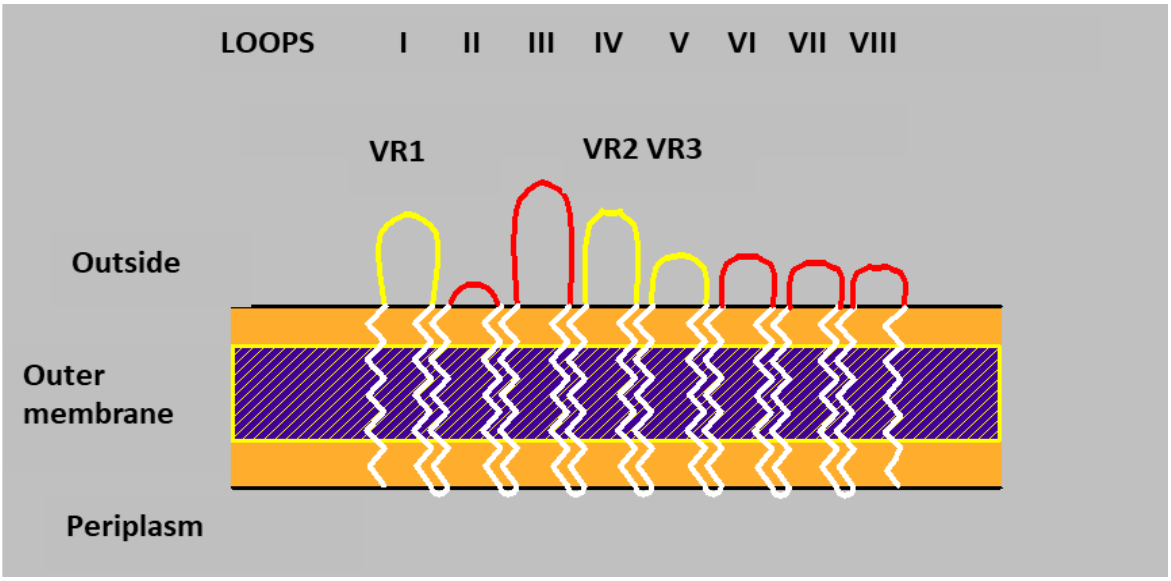
1.3.1.1 Grouping of meningococcal strains

Meningococci can be classified into twelve serogroups, six of which (A,B C, W, X and Y) are responsible for most IMD (Halperin et al., 2012). The serogroup can be determined for culture isolates using the phenotypic methods co-agglutination and dot-blot ELISA, which utilise polyclonal and monoclonal antibodies (Mabs), respectively (Gray et al., 2006). Genotypic methods can be used to determine the genogroup, and are essential for IMD confirmation and group determination in the absence of an isolate (Hackett et al., 2002). PCR assays for genogroup determination target the *siaD* gene for serogroups B, C, W and Y and the *mynA* gene for serogroup A (Hackett et al., 2002). In the MRU, the screening PCR includes detection of the serogroup B determinant gene $siaD_b$. If this is negative, then further PCR assays are used to detect the other common disease-causing serogroups (C [$siaD_c$], W [$siaD_w$], Y [$siaD_y$] and A [*mynA*]).

1.3.1.2 Typing and subtyping of meningococcal strains

The type and subtype of meningococci is derived from variable regions (VRs) in eight surface exposed loops of major OMPs PorB (Class 2 and 3) and PorA (Class 1; P1) respectively (Jolley et al., 2007). Loops I, V, VI and VII give variation in PorB and loops I, IV and V (VRs 1, 2 and 3, respectively) give variation in PorA (Figure 1-1).

Figure 1-1: Variable regions of PorA



Eight (I-VIII) surface exposed loops of PorA and PorB. VR = variable region. PorA variable regions are highlighted.

Traditionally determined using dot-blot ELISA, limited availability of Mabs for recognition of surface exposed epitopes often results in unrecognition of certain variants, deeming isolates non typeable/subtypable (NT) (Wedege and Rosenqvist, 1990). Genotypic methods provide a more sensitive and specific method for typing/subtyping (Sacchi et al., 1998a; Sacchi et al., 1998b).

1.3.1.3 Multi-locus sequence typing

First employed in the 1990s (Maiden et al., 1998), Multilocus sequence typing (MLST) has been a successful method for long-term global surveillance of meningococci.

Owing to high rates of recombination among meningococci, MLST is based on the sequences of seven widely distributed 'housekeeping' genes, which are slow-evolving due to their central role in metabolic function (Urwin and Maiden, 2003). An allelic profile is established and designated a sequence type (ST). STs sharing ≥ four alleles with a predicted founder ST are grouped into clonal complexes (CCs).

The development of an online database (*Neisseria* PubMLST database; *http://pubmlst.org/neisseria*) has enabled the collection and exchange of MLST data worldwide (Jolley et al., 2004).

Whilst MLST is successful in defining population structure, its application in epidemiology is limited, providing no further discrimination between strains of the same ST.

1.3.1.4 Whole genome sequencing

WGS enables discrimination of strains with high genetic similarity. WGS on clinical specimens is not currently routinely performed and sequencing is limited to MLST genes, and more routinely *porA* and *fHbp.* (Diggle and Clarke, 2003; Birtles et al., 2005; Clark et al., 2014).

The first whole genome sequences of *N. meningitidis* strains determined by Sanger sequencing in 2000 were serogroup A and serogroup B (Parkhill et al., 2000; Tettelin et al., 2000). Improvements in sequencing techniques led to the introduction of high-throughput 'next generation' parallel sequencing technology (Harrison et al., 2017). WGS is now routinely used by many public health laboratories across the globe (Köser et al., 2012).

In line with advancements made in sequencing techniques, the storage, accessibility and analytical tools for genomic data have also evolved. The PubMLST database expanded in 2010 with the development of the Bacterial Isolate Genome Sequence Database (BIGSdb) platform, to include WGS data of *Neisseria* isolates (Jolley and Maiden, 2010). As WGS data is deposited into the database, allele numbers are assigned to recognised gene sequences at each defined locus.

This expanding database allows for gene-by-gene pairwise comparisons of isolates using the BIGSdb Genome Comparator Tool (Maiden et al., 2013). Comparisons of 1605 meningococcal 'core genes', defined in pubMLST (cgMLST), which are present among all meningococcal isolates, enable accurate analysis at high resolution (Maiden et al., 2013; Bratcher et al., 2014). Distance matrices based on the number of mismatching genes are

used for phylogenetic analysis, enabling visualisation of genetic relationships between isolates.

WGS is an invaluable method for determining the origins and evolution of virulent strains (Lucidarme et al., 2015) and aids in predicting vaccine strain coverage (Brehony et al., 2015) and establishing the emergence of ABR strains (Mowlaboccus et al., 2017).

1.3.1.5 Antibiotic susceptibility testing

Antibiotic susceptibly testing determines the susceptibility of an organism to antibiotics. It is essential for therapeutic decision making and long-term surveillance of antibiotic susceptibility among meningococci. Several AST methods exist for determination of an isolate's minimum inhibitory concentration (MIC) value; defined as the lowest concentration of an antibiotic required to inhibit the visible growth of an organism under defined test conditions (Andrews, 2001). These include agar dilution, broth dilution and gradient diffusion (Etest) methods. Methods and guidelines vary across laboratories/countries, providing challenges upon interpretation of MIC results (Vázquez et al., 2003; World Health Organization, 2011). MIC results determine the susceptibility category of an organism, which are defined by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) as per Table 1-4.

Table 1-4: Categories of isolates following antibiotic susceptibility testing.

Susceptibility Testing Category	Definition
'Susceptible, standard dosing' **(S)**	Therapeutic success is highly likely where the standard dosing regimen of the antibiotic is used.
'Susceptible, increased exposure' **(I)**	Therapeutic success is highly likely where antibiotic exposure is enhanced by altering the concentration or dosing regimen.
'Resistant' **(R)**	Therapeutic failure is highly likely even with increased exposure.

As defined by EUCAST (European Committee on Antimicrobial Susceptibility Testing, 2019).

The Clinical and Laboratory Standards Institute (CLSI), USA, recommends agar and broth dilution methods and interpretation using CLSI clinical breakpoints (Clinical and Laboratory Standards Institute, 2015). Most European reference laboratories use the gradient diffusion (Etest) method followed by interpretation of EUCAST breakpoints, which is recommended by the European Monitoring Group on Meningococci (Vázquez, 2007). The agar and gradient diffusion (Etest) methods have been shown to be highly comparable, with 100% agreement observed for penicillin (Vázquez et al., 2003). MIC breakpoints of both CLSI (Clinical and Laboratory Standards Institute, 2019) and EUCAST are listed in Table 1-5.

Table 1-5: Breakpoint comparisons: CLSI and EUCAST.

Antibiotic	**Organisation**	**MIC Breakpoint (mg/L)**		
		S*	**I***	**R***
Penicillin	CLSI	≤ 0.06	0.12–0.25	≥ 0.5
	EUCAST	≤ 0.06		> 0.25
Cefotaxime	CLSI	≤ 0.12	-	-
	EUCAST	≤ 0.125	-	> 0.125
Ciprofloxacin	CLSI	≤ 0.03	0.06	≥ 0.12
	EUCAST	≤ 0.03	-	> 0.03
Rifampicin	CLSI	≤ 0.5	1	≥ 2
	EUCAST	≤ 0.25	-	> 0.25

Clinical breakpoint tables of EUCAST and CLSI for interpretation of MICs. * S= Susceptible, standard dosing regimen, I= Susceptible, increased exposure, R= Resistant. CLSI = Clinical Laboratory Standards Institute. EUCAST = European Committee on Antimicrobial Susceptibility Testing.

1.3.2 Epidemiology of invasive meningococcal disease

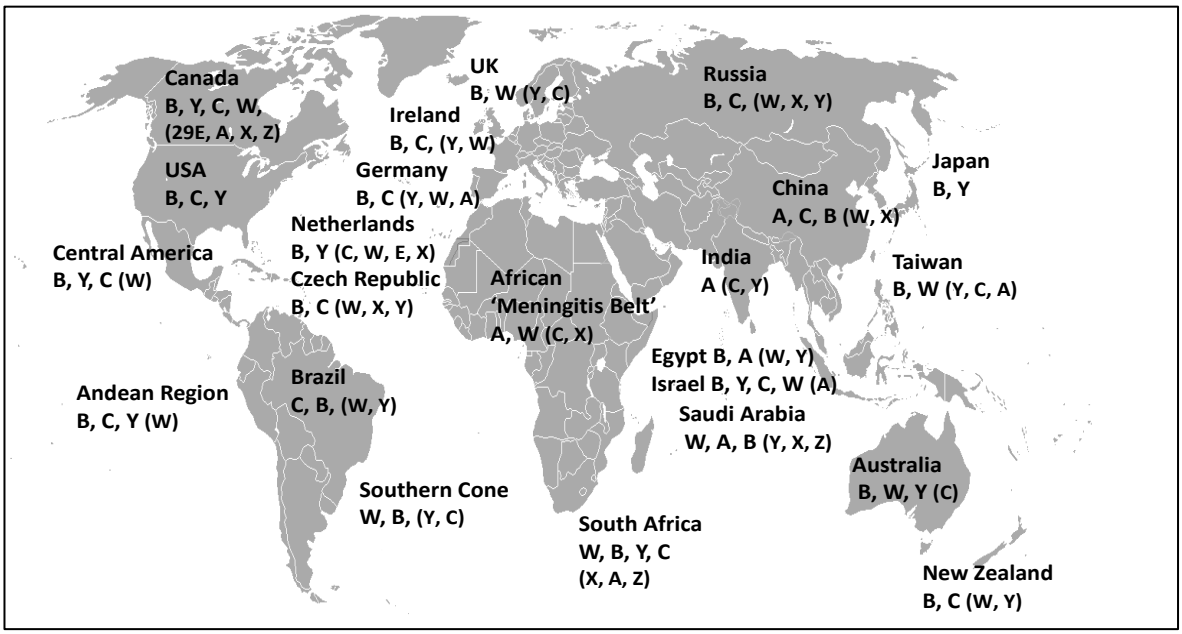
IMD is endemic worldwide, with incidence rates varying with geographical area. In Europe, incidence rates range from 0.45 cases/100,000 in Northern and Southern Europe, to 1.33 cases/100,000 in the UK and Ireland (Parikh et al., 2020). Historically, the 'meningitis belt'

of Sub-Saharan Africa has had the highest incidence of meningococcal disease, with incidence rates as high as 10-1000 cases/100,000 during epidemics, which have occurred frequently in the past. However, following the introduction of a highly effective serogroup A meningococcal vaccine (MenAfriVac) in 2010, meningococcal serogroup A (MenA) disease, previously responsible for most outbreaks in the area, has decreased dramatically (Djingarey et al., 2015; Pelton, 2016; Mustapha and Harrison, 2018; Fernandez et al., 2019). IMD has a case-fatality rate of around 5-10% in developed countries (Hahné et al., 2005; Heckenberg et al., 2008; European Centre for Disease Prevention and Control, 2017), however, this is higher in less developed countries or during outbreaks (Smith et al., 2006; Zunt et al., 2018). IMD affects all age groups with most cases observed among young children, with a second peak in cases in many western countries among adolescents and young adults (Hart and Thomson, 2006).

1.3.2.1 Serogroup distribution

Serogroup distribution of meningococci varies geographically (Figure 1-2), with IMD caused by MenB, MenC and more recently MenW, most prevalent across Europe (Pelton, 2016; European Centre for Disease Prevention and Control, 2017). Following the introduction of the MenA conjugate vaccine in 2010, MenC and MenW outbreaks are primarily reported in the meningitis belt (Centers for Disease Control and Prevention, 2020).

Figure 1-2: Global distribution of disease-causing meningococcal serogroups (Adapted from Millar et al., 2016).



1.3.2.2 Serogroup W disease

Up until the 21st century, the incidence of MenW disease worldwide was low and associated with sporadic cases (Hansman, 1983; Spanjaard et al., 1987; Jackson and Wenger, 1993; Gray et al., 2006). Following the first recorded outbreak of MenW disease in 2000 following the annual pilgrimage to Hajj, Kingdom of Saudi Arabia (KSA), the incidence of MenW disease increased globally (Aguilera et al., 2002)

The Hajj, and other religious mass gatherings, see millions of pilgrims from numerous countries descend on KSA. Crowded conditions facilitate transmission of meningococci and the return of pilgrims to respective countries permits global spread (Yezli et al., 2016).

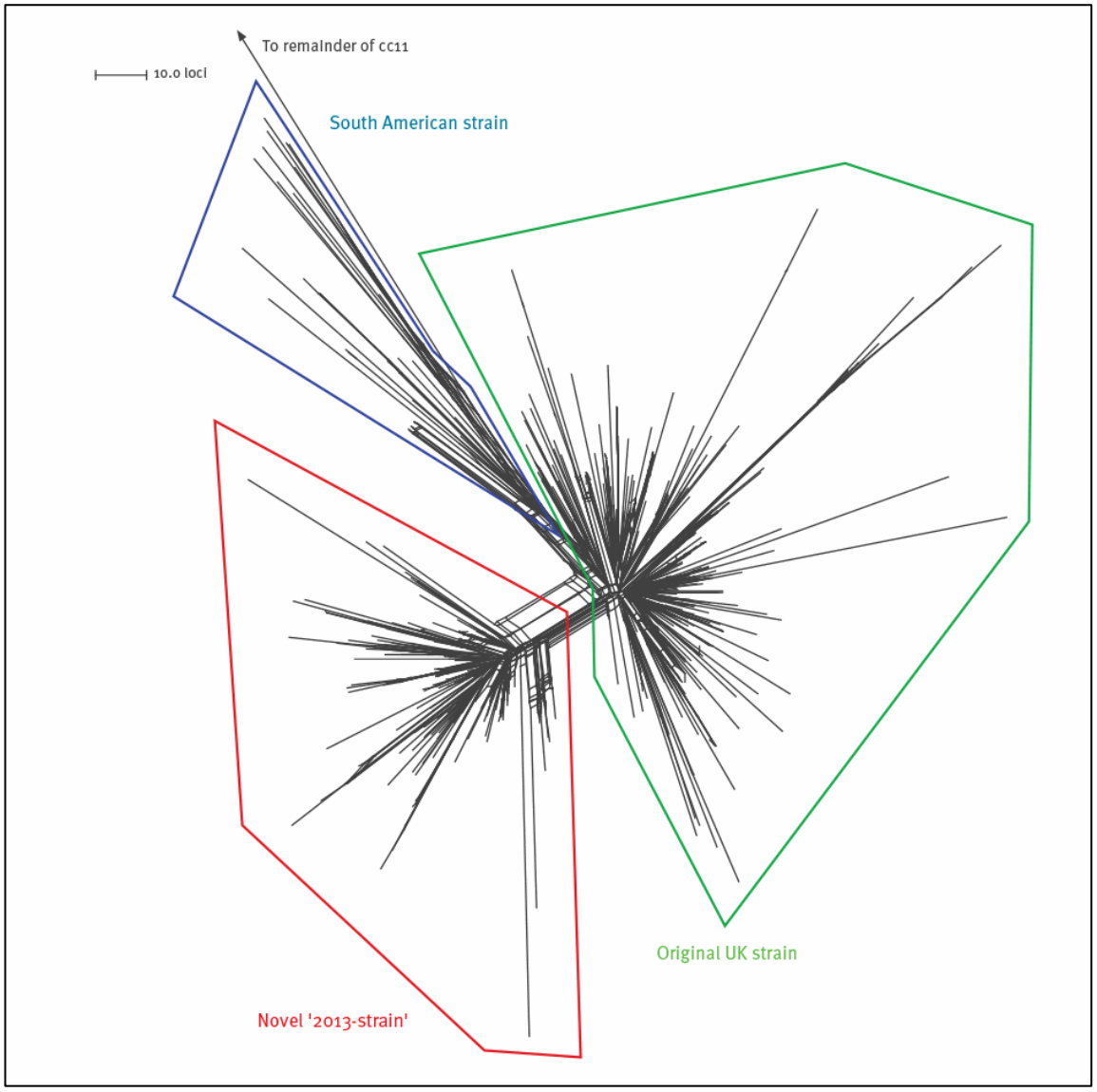
The 2000 Hajj outbreak resulted in localised outbreaks across Europe, Africa, Asia, USA and the Middle East (Fine et al., 2000; Aguilera et al., 2002; Lingappa et al., 2003; Wilder-Smith et al., 2003a; Ceyhan et al., 2012). A similar Hajj-related MenW outbreak in 2001 (World Health Organization, 2001) resulted in mandatory vaccination of subsequent travellers to KSA with the MenACWY plain polysaccharide vaccine, preventing any further major pilgrimage-associated outbreaks (Yezli, Bin Saeed, et al., 2016).

The Hajj outbreak strain was characterised as belonging to the ST-11 CC, and is the predominant MenW lineage in several countries of the Middle East and caused a large outbreak in South Africa between 2003 and 2008 (Abad et al., 2014; Lucidarme et al., 2016; Knol et al., 2017). It has also caused large epidemics in sub-Saharan Africa (Koumaré et al., 2007; Mustapha et al., 2016).

South America observed an increase in IMD caused by a distinct serogroup W ST-11 CC strain from 2003, starting in Brazil (Weidlich et al., 2008), spreading to Argentina and Chile (Sorhouet-Pereira et al., 2013; Araya et al., 2015). The causative strain was genetically distinct from the 'Hajj Outbreak strain', and was termed the 'South American strain' (Lucidarme et al., 2015). The UK observed a rise in MenW disease caused by ST-11 CC isolates from 2009, caused by a descendant of the 'South American strain', and was termed the 'Original UK strain' (Knol et al., 2017). Genomic analysis revealed an additional variant outbreak strain, descended from the 'Original UK strain', emerging in the UK in 2013, termed the 'UK 2013 strain' (Figure 1-3) (Lucidarme et al., 2016). Collectively, the Hajj outbreak strain and related strains belong to the 'Hajj strain sublineage' and the South American strain and related strains belong to the 'South American strain sublineage'.

The 'Original UK strain' and '2013 strain' have spread to Europe, Canada and Australia (Bond et al., 2016; Lucidarme et al., 2016; Martin et al., 2016; Knol et al., 2017; Tsang et al., 2018). Australia identified the emergence of a penicillin-resistant clade of the 'Original UK strain' in 2016, which encompassed isolates from Australia, France, Sweden, the Netherlands and England.

Figure 1-3: The population structure of the South American strain sublineage, including the 'South American strain', 'Original UK strain' and 'UK 2013 strain' (Lucidarme et al., 2016).



CC = clonal complex. The scale bar indicates the number of variable loci between genomes of isolates compared.

1.3.2.3 Non-groupable meningococcal disease and the immunocompromised

IMD caused by unencapsulated meningococci (non-groupable; MenNG) is rare, as capsule absence hinders evasion of the complement system and killing by phagocytosis (Rouphael

and Stephens, 2012). MenNG disease is mainly observed in patients with hereditary or acquired deficiencies of the terminal complement pathway, however, it has also been reported in seemingly immunocompetent individuals (Hoang et al., 2005; Xu et al., 2015).

Acquired complement deficiencies often result from medical conditions and their associated treatments, particularly the use of Eculizumab (Soliris®, Alexion®) to treat atypical haemolytic-uremic syndrome and paroxysmal nocturnal haemoglobinuria (Hillmen et al., 2006; Legendre et al., 2013). A terminal complement pathway inhibitor, Eculizumab prevents the generation of the MAC, also defective in those with inherent deficiencies of the terminal complement pathway. Preventative vaccination is recommended, however cases of IMD have still been reported, including fatal cases (McNamara et al., 2017) (Nolfi-Donegan et al., 2018).

In addition, antibiotic prophylaxis regimes e.g. with penicillin, amoxicillin or ciprofloxacin (Nester et al., 2011; Noone et al., 2012; Struijk et al., 2013) are recommended for immunocompromised patients in certain countries such as the UK and France (Nolfi-Donegan et al., 2018). Penicillin-resistant strains of meningococci have been known to subvert antibiotic prophylaxis regimes in complement deficient individuals (McNamara et al., 2017; Parikh et al., 2017). Antibiotics for rescue therapies may therefore be prescribed (Hawkins et al., 2017; Arnold et al., 2020).

1.4 Antibiotics for meningococcal disease

Antibiotics currently used in the UK for the treatment of meningococcal disease include penicillin, cefotaxime and ceftriaxone. Those used for chemoprophylaxis include ciprofloxacin and rifampicin. The MRU performs AST on isolates for penicillin, rifampicin, ciprofloxacin and cefotaxime.

1.4.1 Beta-lactam antibiotics

Beta-lactam antibiotics, so-called because they contain a beta-lactam ring in their molecular structure (Kong et al., 2010) prevent the synthesis of the peptidoglycan layer of

the bacterial cell wall by binding to one or more penicillin binding proteins (PBPs) of bacteria (Williamson et al., 1986). Beta-lactam antibiotics used in the treatment of IMD include penicillin and the 3GCs cefotaxime and ceftriaxone. Unlike penicillin, 3GCs are less susceptible to degradation by beta-lactamases (Mouton et al., 1979).

1.4.2 Fluoroquinolones

Fluoroquinolones, which contain a fluorine atom in their chemical structure, inhibit DNA replication by targeting two bacterial enzymes essential for the process: DNA gyrase and topoisomerase IV (Hooper, 2001). Each is encoded by two genes; *gyrA* and *gyrB* and *parC* and *parE*, respectively (Drlica and Zhao, 1997). Ciprofloxacin is the fluoroquinolone that is recommended for chemoprophylaxis of IMD.

1.4.3 Ansamycins

Ansamycins are macrocytic antibiotics which have a cyclic structure containing an aliphatic chain connecting two ends of a naphthoquinone core (Maslow and Portal-Celhay, 2015). They inhibit RNA synthesis by binding to the beta subunit of RNA polymerase, encoded by the *rpoB* gene (Wehrli, 1983). Rifampicin is the ansamycin used for chemoprophylaxis of IMD.

1.5 Antibiotic resistance

ABR amongst pathogenic bacteria is deemed one of the most serious public health threats of the 21st century (World Health Organization, 2014). Approximately 700,00 deaths per year are currently attributed to antimicrobial resistance, which without preventative action, is predicted to rise to 10 million deaths per year by 2050 (O'Neill, 2016). Infectious diseases are becoming more difficult to treat due to increasing numbers of resistant bacteria and, with the lack of new antibiotic development, ABR is a worldwide health emergency (Toner et al., 2015).

1.5.1 History

Modern medicine was revolutionised in 1928 following the discovery of the first natural antibiotic, penicillin, by Alexander Fleming (Fleming, 1929) . However, in 1940, resistance to penicillin was first reported, before its widespread use as a therapeutic agent (Abraham, E.P and Chain, 1940; Davies, J & Davies, 2010). The widespread and improper use of antibiotics has accelerated the rate at which resistance has developed and spread. Exposure of bacteria to an array of antibiotics at varying concentrations over decades has provided numerous opportunities for the development of resistant populations.

1.5.2 Mechanisms

Random mutations in bacterial DNA underpins evolution and development of ABR populations by natural selection (Woodford and Ellington, 2007). Acquisition of ABR genes from the environment in previously susceptible bacteria occurs via three main mechanisms of HGT (Table 1-6). Acquired resistance presents the greatest threat, due to increased dissemination of resistance-associated genes between bacteria, occurring at a faster rate than the emergence of resistance through random mutation and natural selection (Peterson and Kaur, 2018).

Table 1-6: Mechanisms of horizontal gene transfer.

HGT Mechanism	Definition
Transformation	Direct uptake and incorporation of exogenous DNA
Transduction	phage transfer of DNA
Conjugation	plasmid-mediated transfer of DNA via cell-to-cell contact

Pathogenic bacteria have developed resistance mechanisms against all classes of antibiotics produced so far (Peterson and Kaur, 2018). Mechanisms include the inactivation or modification of antibiotics, alteration of antibiotic's target sites, limitation of antibiotic uptake and the active efflux of antibiotics from the bacterial cell.

1.5.3 Antibiotic resistance in *Neisseria meningitidis*

Apart from the sulphonamides, which target the bacterial enzyme dihydropteroate synthase preventing folate biosynthesis, meningococci have remained largely susceptible to antibiotics used in IMD treatment. Over the last few decades, concerns over the susceptibility of meningococci to penicillin have been growing and resistance has been observed against other antibiotics used in treatment and prophylaxis. High levels of ABR in the closely related species *N. gonorrhoeae,* adds to concerns that *N. meningitidis* may also develop such levels of resistance, especially given the high capacity for genetic exchange and spread of ABR genes among *Neisseria* species.

1.5.3.1 Penicillin

Meningococci have acquired two resistant mechanisms to penicillin; i) modification of the chromosomally encoded penicillin binding protein 2 (PBP2) which results in a reduced affinity for the antibiotic and ii) antibiotic inactivation by the production of the enzyme, beta-lactamase.

Beta-lactamase production among meningococci is rare. During the 1980s and 1990s, six cases were reported in South Africa, Canada and Spain (MICs of 2 to >256 mg/L (Dillon et al., 1983; Botha, 1988; Fontanals et al., 1989). Plasmids sequenced were almost identical to those from *N. gonorrhoeae*, known to confer penicillin resistance in this species (Bäckman et al, 2000). Plasmid transfer between the two species has been demonstrated *in-vitro*; concerning given their occasional co-existence in the genitourinary tract (Ikeda et al., 1986).

More recently, plasmid-negative beta-lactamase producing penicillin-resistant meningococcal isolates have been identified containing a chromosomally-encoded ROB-1-type beta-lactamase gene (*bla*$_{\text{ROB-1}}$) (Deghmane et al., 2018; Tsang et al., 2019). A recent study in America, identified 33 meningococcal isolates from IMD cases from 2011-2020 containing a *bla*$_{\text{ROB-1}}$ beta-lactamase gene which all belonged to ST-23 CC (McNamara et al., 2020). *Bla*$_{\text{ROB-1}}$ is almost identical to a DNA fragment found in a plasmid (pB1000) of

Haemophilus influenzae (Tsang et al., 2019) known to cause resistance to beta-lactams in this and other species (San Millan et al., 2007, 2010).

Non-beta-lactamase producing IMD isolates with reduced susceptibility to penicillin were first reported in 1985 (Van Esso et al., 1987). Resulting from alterations in the structure of PBP2 (PubMLST locus NEIS1753), levels of resistance are lower than that of beta-lactamase producing meningococci and is now the most frequently observed mechanism associated with reduced susceptibility and resistance to penicillin among meningococci (Sáez-Nieto et al., 1992; Tzanakaki et al., 1992; Lopardo et al., 1993; Woods et al., 1994; du Plessis et al., 2008; Hedberg et al., 2009; Gorla et al., 2018a; Vacca et al., 2018).

Alterations in PBP2 conferring reduced susceptibility or resistance to penicillin are located in C-terminal half of the protein; a 402 bp fragment of NEIS1753, encoded by a gene fragment designated *penA* (Thulin et al., 2006). *PenA* alleles of penicillin-susceptible meningococcal isolates are uniform in DNA sequence compared to those of resistant isolates, which have a mosaic structure made up of sections that are the same as those found in susceptible isolates and sections that are highly variable (Spratt et al., 1992). HGT between meningococci and commensal *Neisseria* species e.g. *Neisseria flavescens*, which are intrinsically more resistant to penicillin (Zapun et al., 2016), has enabled susceptible meningococci to replace parts of their *penA* genes, producing altered forms of PBP2 and reducing affinity to penicillin.

Five amino acid substitutions (AASs) are usually always present in the *penA* gene of isolates with reduced susceptibility or resistance to penicillin; F504L, A510V, I515V, H541N, and I566V (Taha et al., 2007). Reduced penicillin susceptibility has also been observed among meningococcal isolates harbouring a *penA* gene with only four of these substitutions; *penA*327 (Zapun et al., 2016), with additional AASs I312M, V316T, N512Y and G545S.

PenA327 has also been associated with reduced susceptibility to the 3GC, cefotaxime (Deghmane et al., 2017).

1.5.3.2 Cefotaxime and ceftriaxone

Only one study has reported meningococcal resistance to 3GCs, with six MenA isolates from IMD cases in India displaying resistance to ceftriaxone (MICs = 0.25-8 mg/L) and cefotaxime (MICs = 0.5->32 mg/L) (Manchanda and Bhalla, 2006). No further characterisation of these isolates was performed despite requests from researchers who challenged the methods used for species confirmation (gram staining and latex agglutination only) (Nicolas, 2007).

Recently, reduced susceptibility to cefotaxime has been reported among IMD isolates in France (n=25; MICs = 0.047-0.125 mg/L), which also displayed reduced susceptibility or resistance to penicillin (0.125-0.38 mg/L) (Deghmane et al., 2017). All isolates harboured *penA327*, proven to be responsible for reduced susceptibility to 3CGs in meningococci when transformed into a 3GC susceptible isolate.

PenA327 has previously been identified among meningococcal isolates in men who have sex with men, and in patients with meningococcal urethritis (Taha et al., 2016; Deghmane et al., 2017). The allele is identical in sequence to an allele found among *N. gonorrhoeae* with increased resistance to 3GCs (PBP2 XXXIV) (Ohnishi et al., 2011), and suggestions have been made regarding meningococcal acquisition of the allele during co-colonisation in the genitourinary tract (Deghmane et al., 2017). An additional AAS in PBP2 XXXIV, A501P, which has been shown to further enhance levels of 3GC resistance among gonococci, has raised concerns regarding the selection of the same mutation among meningococci (Zapun et al., 2016).

1.5.3.3 Ciprofloxacin

Ciprofloxacin resistance is caused by mutations in the *gyrA* gene, altering the antibiotic target site to prevent binding.

Since ciprofloxacin resistance was first observed among meningococci in 1992 (Tzanakaki et al., 1992), it has been infrequently reported, mainly associated with sporadic cases among diverse isolates (Shultz et al., 2000; Alcalá et al., 2004; Skoczyńska et al., 2008;

Lapadula et al., 2009; Zhu et al., 2014; Gorla et al., 2018b; Vacca et al., 2018). Ciprofloxacin resistance remains rare worldwide, except for China, where its prevalence has resulted in withdrawal of its use as a first line prophylactic agent (Zhu et al., 2014; Chen et al., 2015). A high proportion of ciprofloxacin-resistant meningococci in China belong to the ST-4821 CC, a hyperinvasive strain in this country (Zhu et al., 2014, 2015). Other countries have also reported ciprofloxacin-resistant isolates belonging to this CC (Tsang et al., 2017; Kawasaki et al., 2018). In India, ciprofloxacin-resistant MenA strains emerged from an outbreak of IMD in 2005 (Singhal et al., 2007), and in the US, a cluster of three MenB ciprofloxacin resistant isolates belonging to ST-162 CC was reported in 2007-2008 (Wu et al., 2009). More recently, eleven ciprofloxacin-resistant isolates belonging to ST-23 CC were identified in the US, which were also penicillin-resistant due to the production of beta-lactamase owing to the $Bla_{\text{ROB-1}}$ gene (McNamara et al., 2020). In 2019, three cases of meningococcal disease caused by a ciprofloxacin-resistant NG ST-175 CC strain were identified in England, linked to travel to Mecca, KSA (Public Health England, 2019; Willerton et al., 2020).

Ciprofloxacin resistance among meningococci is mainly attributed to point mutations in the quinolone-resistance-determining region of the *gyrA* gene. The most common among meningococci is a single AAS; T91I or D95N (Hong et al., 2013). Other AASs in the *gyrA* gene of ciprofloxacin-resistant meningococci have been less frequently reported (A103A, I111V and V120I) (Tsang et al., 2017; Villalba et al., 2008).

Mutations in the *parC* gene have been observed among ciprofloxacin-resistant meningococci, however always accompanied by *gyrA* AAS T91I (Kawasaki et al., 2018; Chen et al., 2020). Chen and colleagues demonstrated that while mutations in *ParC* are not sufficient alone to confer ciprofloxacin resistance among meningococci, they result in enhanced levels of resistance when present in conjunction with altered *gyrA* genes (MICs 0.5-1.0 mg/L) (Chen et al., 2020).

It has been suggested that ciprofloxacin resistance-associated *gyrA* alleles originate from commensal *Neisseria* species, including *Neisseria lactamica* and *Neisseria cinerea*, highlighting the significance of HGT amongst *Neisseria* and its role in ABR among meningococci (Wu et al., 2009; Chen et al., 2020).

1.5.3.4 Rifampicin

Meningococcal resistance to rifampicin results from single point mutations in the central region of the *rpoB* gene (Carter et al., 1994) preventing binding of rifampicin to RNA polymerase (Hartmann et al., 1967).

Resistance among meningococci is associated with AASs at amino acid (AA) position 552, with AASs at other positions also reported (542, 548 and 557) (Taha et al., 2010). Significantly different levels of rifampicin resistance (MICs 8-256 mg/L) have been observed among strains with the same *rpoB* mutations, suggesting that other factors may contribute to rifampicin resistance (Carter et al., 1994; Stefanelli et al., 2001; Taha et al., 2010). Mutations in the *mtrR* gene and its promoter region, which encode a transcription repressor of the mtrCDE efflux pump (Skoczynska et al., 2009) have been associated with high levels of rifampicin resistance among *N. gonorrhoeae* (Hagman et al., 1995). Whilst *N. meningitidis* isolates generally possess a functional mtrCDE efflux pump, its regulation and expression appears to differ from that of *N. gonorrhoeae* (Rouquette-Loughlin et al., 2004), with no evidence suggesting that such mutations confer resistance among *N. meningitidis* (Abadi et al., 1996; Skoczynska et al., 2009).

Rifampicin resistance is rare among invasive meningococci, more frequently reported in isolates from secondary cases following the use of rifampicin for chemoprophylaxis (Berkey et al., 1988; Almog et al., 1994; Dawson et al., 1999; Rainbow et al., 2005; M. Taha et al., 2006b). Reports of rifampicin resistance among IMD strains of index cases have however been reported (Stefanelli et al., 2001; Rainbow et al., 2005). Rifampicin resistance has been reported across diverse meningococcal isolates and lack of clonal expansion of resistant strains suggests mutations in *rpoB* may have major biological costs for meningococci (Taha et al., 2006b; Colicchio et al., 2015).

1.6 Aims and objectives

The PHE MRU has MIC and WGS data from all invasive IMD case isolates in E, W and NI from July 2010, however, this has yet to be reviewed collectively and systematically analysed. The primary aims of this project were to:

1) Provide a timely review of ABR among IMD isolates received at the MRU from epidemiological years 2010/11-2018/19.
2) Investigate ciprofloxacin resistance amongst isolates of the ST-175 CC following an outbreak of meningococcal disease caused by ciprofloxacin-resistant ST-175 CC isolates in England, 2019.
3) Investigate the observed increase of penicillin resistance among English serogroup W ST-11 CC IMD isolates.

2 Materials and Methods

Each of the methods described here have been performed personally for the generation of data included in this study. MIC and WGS data were obtained continuously by colleagues of the MRU, including myself, as isolates were received. All MIC and WGS data obtained prior to January 2018 were generated by other MRU colleagues. All PCR and sequencing data, the obtainment of genomic data, and phylogenetic analyses conducted in this study were performed solely by me.

2.1 Isolate/genome panels

2.1.1 Panel 1

Panel 1 (n=4,122; Appendix 1) was used to investigate ABR among all IMD isolates received at the MRU and whose genomes were available on the MGL database (accessed 29/06/2020), from E, W and NI from epidemiological years (July-June) 2010/2011 (n=500), 2011/2012 (n=400), 2012/2013 (n=450), 2013/2014 (n=403), 2014/2015 (n=505), 2015/2016 (n=521), 2016/2017 (n=501), 2017/2018 (n=488) and 2018/2019 (n=354) (section 3.1). These comprised blood culture (n=3,730), CSF (n=279), joint (n=101), brain (n=3), pericardium (n=3), bone marrow (n=2), pus/hip (n=2), spleen (n=1) and chest drain (n=1) isolates.

2.1.2 Panel 2

Panel 2 (n=79; Appendix 2) was used to investigate a recent cluster of IMD/conjunctivitis cases involving ciprofloxacin-resistant ST-175 CC isolates in England (section 3.2). It comprised English invasive (n=2; 2015 & 2019) and conjunctivitis (n=2; 2019) ST-175 CC isolates/genomes received at the MRU, carriage genomes from two UK carriage studies (n=6; 2015-2018) (Carr et al., 2018; Bratcher et al., 2019), and ST-175 CC genomes of IMD isolates from South Africa (n=16; 2003-2017), Germany (n=4;2016-2019), Italy (n=3; 2014-2018), Burkina Faso (n=2; 2012), Spain (n=2; 2002 & 2005), France (n=1; 2012), Sweden (n=1; 2016) and Togo (n=1; 2007). The panel also included genomes of carrier isolates or

isolates with unknown disease status from Ethiopia (n=10; 2014), Niger (n=3; 2003-2006), Norway (n=3; 2018-2019), Benin (n=2; 2006-2007), Burkina Faso (n=2; 2008-2010), Italy (n=2; 2016), Brazil (n=1; 2014), France (n=1; 2016), South Africa (n=1; 2003), Spain (n=1; 2018), Togo (n=1; 2007) and USA (n=1; 2000). Other closely related genomes included in this panel with at least four ST-175 MLST alleles were unassigned to a clonal complex (n=9) or had incomplete MLST profiles (n=2).

2.1.3 Panel 3

Panel 3 (n=897; Appendix 1, n=879 and Appendix 3, n=18) was used to investigate penicillin resistance amongst English invasive serogroup W ST-11 CC isolates (section 3.3). It comprised English invasive serogroup W ST-11 CC isolates (n=867) and closely related isolates/genomes with at least four ST-11 MLST alleles (n=30) received at the MRU between July 2010 and August 2019. To investigate penicillin resistance among serogroup W ST-11 CC isolates in a wider context, also included were invasive/carrier serogroup W ST-11 CC genomes from PubMLST closely related to English invasive PenR serogroup W ST-11 CC isolates/genomes including genomes from New Zealand (n=35; 2017-2018), Canada (n=22; 2014-2019), Ireland (n=12; 2013-2019), Scotland (n=10; 2015-2020), Spain (n=10; 2017-2020), Sweden (n=8; 2016-2019), The Netherlands (n=7; 2016-2019), Germany (n=6; 2018-2019), France (n=4; 2016-2018), Wales (n=4; 2015-2019), Chile (n=2, unknown), Finland (n=2; 2015), Italy (n=2; unknown & 2014), Greece (n=1; 2017), Japan (n=1; 2017), Northern Ireland (n=1; 2016), Portugal (n=1; 2019), UK (n=1; unknown) and USA (n=1; 2009).

2.2 Storage/culture of isolates

All meningococcal cultures received at PHE's MRU since July 2010 underwent routine receipt, culture, species confirmation, characterisation (including AST and WGS) and archiving.

All manipulations of live cultures and suspensions were performed in a Class 1 safety cabinet within a category 2+ laboratory. Fresh cultures of meningococcal isolates were prepared from cultures, submitted by diagnostic laboratories or archived cultures, on

Columbia blood agar (CBA) (Oxoid, UK). Archived cultures were stored on Microbank® beads (Prolab Diagnostics, Canada) or Microorganism Preservation System - Protect beads (Technical Service Consultants Ltd, Lancashire, UK) at -80°C. Fresh cultures were incubated overnight (16-24 hours) at 37°C under 5% CO_2. The following day, plates were checked for purity and subcultured to CBA where necessary.

2.2.1 Streak plate for isolated colonies

Using a 10 µL sterile loop (Sarstedt, Germany), the desired inoculum (diagnostic laboratory submitted, subculture or archived culture) was initially spread in a tight streak across the first quadrant of the agar plate. Using the same loop, streaks were then drawn from the preceding area into the next quadrant until the fourth quadrant was reached. A final streak was made downwards towards the centre of the plate in a zigzag motion.

2.2.2 Lawns for antibiotic susceptibility testing

Following overnight incubation of a streak plate (section 2.2.1), approximately five isolated colonies were selected using a sterile swab and inoculated in five millilitres of sterile water contained in a glass bijou (Oxoid, UK) to achieve a suspension turbidity of McFarland standard 0.5 (visually determined using McFarland standard set; 0.5-4.0). The swab was gently pressed against the inside wall of the bijou and then used to spread the inoculum over the entire surface of a Mueller Hinton agar plate supplemented with 5% horse blood and 20 mg/L β-nicotinamide adenine dinucleotide (Oxoid, UK; Isolates received after 9th May 2019) or Iso-sensitest blood agar supplemented with 5% (v/v) defibrinated horse blood and 20 mg/L NAD (Oxoid, UK; Isolates received prior to 9th May 2019). Spreading was repeated three to four times with the plate rotated 90° each time to ensure even distribution and full coverage. The plate was left to dry for five to ten minutes at room temperature (RT) to remove excess moisture.

2.3 Antibiotic susceptibility testing

Antibiotic susceptibility testing was performed using gradient diffusion methodology using Etest (bioMerieux UK Limited, UK) or MIC Evaluator (Oxoid, UK) strips coated with predefined gradients of antibiotics. For each isolate, MICs for both therapeutic (penicillin and cefotaxime) and prophylactic (rifampicin and ciprofloxacin) antibiotics were determined.

A lawn was prepared (section 2.2.2) and the appropriate gradient diffusion strip was placed in the centre of the plate using sterile forceps in accordance with the manufacturer's instructions. The plate was incubated overnight (16-24 hours) at 37°C under 5% CO_2.

MIC values were recorded at half-dilutions for epidemiological purposes as opposed to doubling dilutions for clinical interpretation. MIC values were interpreted according to EUCAST guidelines (Table 1-4; EUCAST; v10.0; 2020-01-01) (European Committee on Antimicrobial Susceptibility Testing, 2019).

2.3.1 Beta-lactamase testing

Using sterile forceps, an Interlactam strip (MAST, UK) was placed in the centre of an empty petri dish. A drop of sterile water was added to each area of the strip using a sterile disposable pastette. Following overnight incubation of a steak plate (section 2.2.1), a loop full of the test culture was added to the appropriate test area on the Interlactam strip using a 10 µL sterile loop. Following the overnight incubation of streak plates of both negative (beta-lactamase negative *N. meningitidis*) and positive (beta-lactamase positive *Haemophilus influenzae*) control organisms, a loop full of each were added to the appropriate control areas of the Interlactam strip using a fresh 10 µL sterile loop. The strip was incubated at room temperature for one hour and a colour change was observed for positive reactions.

2.4 DNA extraction

For PCR and DNA sequencing, heated DNA extracts were prepared (section 2.4.1). DNA extraction from meningococcal isolates for WGS was performed using either the Wizard Genomic DNA Purification Kit (Promega, WI, USA) for up to 24 samples (section 2.4.2) or the MagMax DNA multi sample ultra-kit (Thermo Fisher Scientific, MA, USA) with the Kingfisher flex Purification System (Molecular Devices, CA, USA) for >24 samples (section 2.4.3).

2.4.1 Heated DNA extracts

Following overnight incubation of a streak plate (section 2.2.1), 10-15 colonies were collected using a sterile swab and emulsified in two millilitres sterile saline contained in a glass bijou (Oxoid, UK). Two hundred and fifty microliters of the suspension were then transferred to a 1.5 mL microtube and heated at 100°C for 10-11 minutes. The microtube was then snap chilled at -20°C for five to six minutes and centrifuged at 12,000 g for five minutes. The supernatant was then collected using a sterile fine-tipped pastette, retained and stored at 4°C.

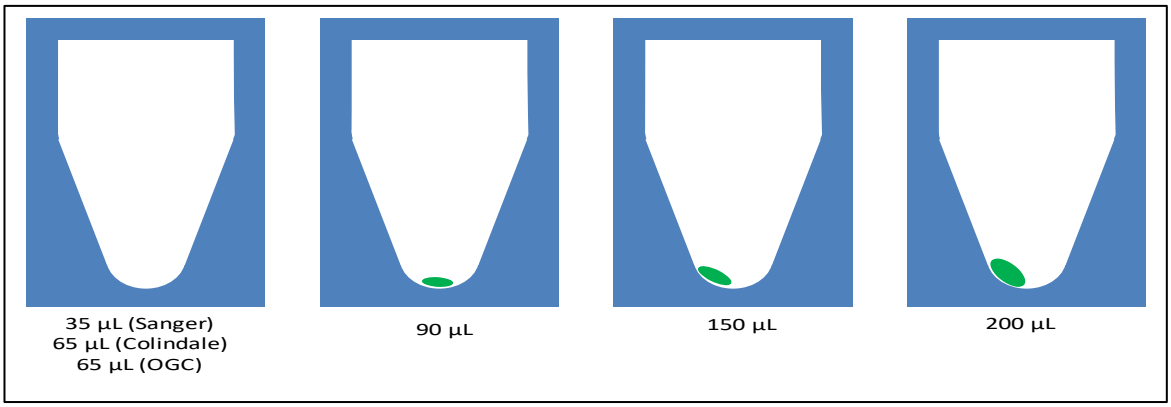
2.4.2 Lawns for DNA extraction

Lawns were prepared from archived cultures using a 10 µL sterile loop to obtain a single bead or loop full of frozen inoculum and spread in a ~5mm thick line across the centre of a CBA plate. The plate was rotated 90° and the inoculum was spread from top to bottom evenly across the whole surface ensuring not to touch the sides to achieve a semiconfluent lawn.

2.4.3 DNA extraction – Promega Wizard

Using a sterile swab, eight full length sweeps of overnight growth (section 2.2.2) were suspended in 250 µL of saline (Oxoid, UK) to a turbidity ≥ McFarland 4 (visually determined using McFarland standard set; 0.5-4.0). Fifty microlitres of suspension was transferred to a 1.5 mL microtube containing 550 µL nuclei lysis solution using a pipette and mixed thoroughly. The microtube was transferred to an 80°C heating block for five minutes and then cooled to RT for 10-11 minutes. Following a pulse spin (button released at 5000 rpm), three microlitres of RNase solution was added to the tube which was then inverted several times to mix. Following a pulse spin (button released at 5000 rpm) the microtube was incubated at 3°C for 15 minutes. Once cooled to RT, the tube was centrifuged using a pulse spin (button released at 5000 rpm) before 200 µL protein precipitation solution was added. The microtube was then vortexed for 20 seconds to mix. Following incubation in a cool box (-20°C cooling cartridge with 4°C aluminium block) for five minutes, the tube was vortexed for two seconds and centrifuged at 16,000 g for three minutes. The supernatant was discarded and 600 µL of 70% v/v ethanol added. The tube was inverted several times to mix and centrifuged at 16,000 g for two minutes. The supernatant was carefully removed leaving a DNA pellet for which, size/external sequence provider dependant, the appropriate volume of DNA rehydration solution was added to achieve a DNA concentration suitable for WGS (Figure 2-1).

Figure 2-1: A guide of DNA rehydration solution volume versus DNA pellet size to achieve a DNA concntration suitable for genome sequence analysis.



DNA pellet = green oval. White tube = 1.5 mL microtube. OGC = Oxford Genomics Centre. Sanger, Colindale and OGC = external sequence providers.

2.4.4 DNA extraction - Kingfisher flex purification system

Using a sterile swab, eight full length sweeps of overnight growth (section 2.2.2) were suspended in 200 µL of saline (Oxoid, UK) to a turbidity ≥ McFarland 4 (visually determined using McFarland standard set; 0.5-4.0).

Twenty-five microlitres of suspension were transferred to a microtube containing 200 µL proteinase K mix (8 µL of proteinase K and 192 µL of PK buffer) using a pipette and mixed thoroughly. The microtube was transferred to a 60°C water bath for 60-70 minutes before cooling at RT for 10-11 minutes. Following a pulse-spin (button released at 5000 rpm), 24 µL of RNase solution (1.2% v/v RNase in molecular grade water) was added to the tube and vortexed at ~1800 rpm for approximately 10 seconds, inverting the tube twice throughout. Following a pulse spin (button released at 5000 rpm), 456 µL of lysis solution (200 µL multi-sample lysis buffer, 16 µL DNA binding beads and 240 µL isopropanol [Sigma-Aldrich, UK]) was added and mixed gently but thoroughly until homogenous using the pipette. The lysate was then transferred to a well of a 96 deep well plate (Thermo Fisher Scientific, MA, USA) for loading onto the KingFisher Flex Purification System.

Other plates used in the extraction (all 96 deep well plates) included an elution plate prepared by adding 150 µL AE elution buffer (Qiagen, Germany) or 75 µL of elution buffer 1 and elution buffer 2 per well, wash plate 1 prepared by adding 150 µL of wash solution 1 per well and wash plates 2 and 3, prepared by adding 150 µL of wash solution 2 per well.

DNA extracts were transferred to a microamp optical 96 well reaction plate (Thermo Fisher Scientific, MA, USA) on a dynamag side skirted magnet (Thermo Fisher Scientific, MA, USA) for 15-20 minutes to remove residual beads. The extracts were then transferred using a multichannel pipette to a fresh microplate and sealed with microamp strip caps (Thermo Fisher Scientific, MA, USA).

2.5 DNA Quantification

DNA quantification was performed using the SptectraMax Quant AccuBlue HiRange dsDNA assay kit (Molecular Devices, CA, USA) with the SpectraMax M5e plate reader (Molecular

Devices, CA, USA) or using the Qubit dsDNA BR assay kit (Thermo Fisher Scientific, MA, USA) with the Qubit 2.0 (Thermo Fisher Scientific, MA, USA).

2.5.1 SpectraMax

Standards and samples were pre-mixed as appropriate (vortex or gentle pipetting) and centrifuged using a pulse spin (~5000 rpm). Working solution 1 was prepared by diluting Accublue Hirange dye 1:100 in Accublue Hirange buffer. Working solution 2 was prepared by diluting Accublue Hirange enhancer 1:100 in working solution 1. Ten microlitres of each kit standard (0, 2, 6.25, 12.5, 25, 20, 100, 150, 200 ng/µL) was added to the wells of a Greiner black polystyrene flat-bottom 96 well microplate (Sigma-Aldrich, UK) in duplicate. Ten microlitres of each sample was transferred to the remaining wells. Two hundred microlitres of working solution 2 was added to active wells and gently mixed. The plate was sealed with microplate sealing tape (Thermo Fisher Scientific, MA, USA), wrapped in aluminium foil and incubated at RT for 5-10 minutes. The foil and seal were removed, and the plate was placed in the plate reader and fluorescence measured with excitation at 350 nm and emission at 460 nm.

2.5.2 Qubit

Qubit solution was prepared by diluting dsDNA BR reagent 1:200 in Qubit dsDNA BR buffer in a suitable container (microtube or universal tube) as per number of samples. One hundred and ninety-five microlitre of Qubit solution was transferred into appropriately labelled 0.5 mL PCR tubes (Thermo Fisher Scientific, MA, USA) for the samples and 190 µL was transferred to labelled microtubes for the two standards (0, 100ng/µL). Five microlitres of each sample and 10 µL of each standard were added to the corresponding tubes and vortexed (~750 rpm for three seconds). The tubes containing the standards were inserted into the Qubit reader and concentrations recorded to generate a standard line. Each sample was then inserted, and the concentration of each sample recorded on completion of measurement.

2.6 Whole genome sequencing

Extracts were sent to external sequence providers (The Sanger Institute, PHE Genomic Services or the Oxford Genomics Centre) for WGS on the Illumina HiSeq platform after adjusting to the required DNA concentration for the sequence provider (20 ng/µL, 6-100 ng/µL, 30-50 ng/µL, respectively). Sequence data were then transferred to the Maiden laboratory at the University of Oxford for assembly and inclusion on the PubMLST *Neisseria* database and the Meningitis Research Foundation (MRF) Meningococcus Genome Library (MGL; https://pubmlst.org/bigsdb?db=pubmlst_neisseria_mrfgenomes), a distinct project within the PubMLST *Neisseria* database.

2.7 Obtaining genomic data

2.7.1 Genomic data from MGL/PubMLST

Genomic data for IMD isolates received at the MRU were accessed from the MGL. Genomic data for non-invasive meningococcal isolates received at the MRU and genomic data for meningococcal isolates from other countries were accessed from the PubMLST *Neisseria* database. Associated metadata (e.g. country, year, number of contigs per genome, total genome length and MICs where available) and genotypic data (e.g. allele IDs for *PorA, NadA*, *nhba,* fHbp variant, fHbp peptide and MLST data) were exported from the MGL database or PubMLST *Neisseria* database using the 'export dataset' function.

2.7.2 BLAST searches

BLAST searches were performed using the BLAST function on the PubMLST *Neisseria* database. The isolate ID and query sequence were pasted into the search box and the required number of hits and length of flanking sequence were selected. Sequences were exported as FASTA files.

2.7.3 Identifying genes broken between contigs

Where genes were broken between different contigs, corresponding hits were exported in FASTA format for alignment with a reference sequence (section 2.7.4). Provided there was complete homology in the overlapping region, which was at least 10 bp in length, the sequences were trimmed, ligated and used in a sequence query (section 2.7.5). If there was a discrepancy in the overlapping region, or if it was less than 10 bp in length, PCR and Sanger sequencing were performed (section 2.8).

2.7.4 Sequence alignments

Multiple sequence alignments were performed using BioEdit (Version 2.7.5.0, Hall, 1999) either manually by eye or using the ClustalW tool with default settings followed by manual adjustment. Alternatively, multiple sequence alignments or alignment of contiguous sequences were performed using the 'align automatically' feature of Sequencher (version 4.7; Gene Codes Corporation, MI, USA).

2.7.5 Sequence query

To identify an allele ID, the query sequence was pasted into the query sequence tool on the PubMLST *Neisseria* database. If the search returned no exact match, the sequence was submitted to the database as a new allele (section 2.7.6).

2.7.6 Sequence submission

Sequences of new alleles were submitted to the PubMLST *Neisseria* database for verification and allele assignment by a database curator. The 'submit alleles' function and appropriate loci were selected and the FASTA sequence entered into the sequence box. New sequences arising from Sanger sequencing (section 2.8) were submitted along with generated raw AB1 files (section 2.8.2.4).

2.8 PCR and sequencing of *penA*

Where isolates were missing allele IDs for *penA* genes and where BLAST searching failed to identify the gene sequence, PCR and Sanger sequencing were performed.

2.8.1 PCR

2.8.1.1 Primer Preparation

Primers were received lyophilised (Eurofins Genomics, Germany) and reconstituted in molecular grade water to a master stock concentration of 100 µM as per the manufacturer's datasheet. Working stocks (5 µM) were prepared by diluting master stocks 1/20 in molecular grade water.

2.8.1.2 PCR master mix preparation

PCR master mix was prepared within a PCR cabinet in a clean room using the HotStar Taq DNA polymerase kit and dNTP mix (Qiagen, Germany). The reagents were added to a sterile universal tube (Table 2-1) and mixed thoroughly using a sterile pipette. Twenty-three microlitres of master mix was transferred to the wells of a MicroAmp optical 96-well reaction plate (Thermo Fisher Scientific, MA, USA).

Table 2-1: PCR master mix reagents.

Primer details	
PenA Forward primer (PenA1F)*	5'-gttttcccagtcacgacgttgtaATCGAACAGGCGACGATGTC-3'
PenA Reverse primer (PenA1R)*	5'-ttgtgagcggataacaatttcGATTAAGACGGTGTTTTGACGG-3'
Reagent volumes (µL per 1X reaction)	
10x PCR buffer	2.5
Primer PenA1F (5 µM)	2.5
Primer PenA1R (5 µM)	2.5

dNTPs (10 mM)	0.5
Taq polymerase (5 units/µL)	0.125
Molecular water	14.125
$MgCl_2$ (25 mM)	0.8
Total	23.05

Volumes of mastermix reagents used in the *penA* PCR assay. *Universal forward/reverse sequences (lowercase) added as adapters and used as sequencing primers as previously described by Taha *et al*. (Taha *et al*., 2007).

2.8.1.3 Addition of DNA extracts and reaction

DNA extracts (section 2.4.1) were spun using a pulse spin (button released at 5000 rpm). One microlitre of each extract was added to the corresponding wells of the PCR reaction plate containing the master mix using a sterile pipette. Microamp cap strips were used to seal the plate which was then transferred to a thermal cycler and run under the conditions listed in Table 2-2.

Table 2-2: PCR thermal cycler conditions.

Stage		**Temperature (°C)**	**Time**
Taq activation		95	15 minutes
Denaturation	x35 cycles	95	30 seconds
Annealing		59	30 seconds
Extension		72	130 seconds
Final extension		72	7 minutes
Holding		4	∞

PCR thermal cycler conditions of the *penA* PCR assay.

2.8.1.4 Visualisation of PCR products

Gel electrophoresis was performed to establish the presence of amplified products. A 2% agarose gel was prepared by adding three grams of agarose (Sigma-Aldrich, UK) to 150 mL 1x Tris-Borate EDTA buffer (Sigma-Aldrich, UK) and heating in a microwave until fully dissolved. Fifteen microlitres of SYBR Safe DNA stain (Thermo Fisher Scientific, MA, USA) was then added and mixed. The dissolved agar was poured into a casting tray with gel combs and left to set at RT. The gel was transferred to a gel tank and covered with 1x TBE buffer.

Five microlitres of gel loading buffer (30% v/v glycerol solution with a small amount of Bromophenol blue [Sigma-Aldrich, UK]) was mixed with five microlitres of each PCR product and loaded into the wells of the agarose gel using a sterile pipette. Ten microlitres of ExACTGene low range plus DNA ladder (Thermo Fisher Scientific, MA, USA) was loaded per row. The gel was run at 130 volts for 15-20 minutes. The gel was visualised using the G:BOX transilluminator (Syngene, MD, USA).

2.8.1.5 Clean-up of PCR products

Two microlitres of Exo-SAP-IT (Thermo Fisher Scientific, MA, USA) were added to the wells of a MicroAmp fast optical 96-well reaction plate (Thermo Fisher Scientific, MA, USA). Five microlitres of each PCR product was transferred to the wells using a sterile pipette, mixed thoroughly and sealed using MicroAmp cap strips. The plate was transferred to an ABI 9800 Fast thermal cycler (Applied Biosystems, MA, USA) and heated at 37°C for 15 minutes then at 80°C for 15 minutes. The plate was removed and 21 µL of molecular grade water was added to each of the active wells.

2.8.2 Sanger Sequencing

2.8.2.1 Sequencing primer preparation

Sequencing primers were prepared as detailed in section 2.8.1.1.

2.8.2.2 Sequencing master mix preparation

Sequencing master mix was prepared per primer using the BigDye terminator v3.1 cycle sequencing kit (Thermo Fisher Scientific, MA, USA). The reagents were added to sterile 1.5 mL microtubes (Table 2-3).

Table 2-3: Sequencing master mix reagents.

Reagent	**Volume (µL per 1x reaction per primer)**
Molecular water	6.09
Sequencing primer 5 µm (UniF/UniR)*	0.66
ABI 5x sequencing buffer	1.75
ABI bigdye v3.1	0.5
Total	9

Volumes of sequencing reagents used in the *penA* PCR and sequencing assay. * As described by Taha *et al*. (Taha et al., 2007)

Nine microlitres of master mix was added to a Microamp 96 well plate. One microlitre of each cleaned up PCR product was added to the master mix and transferred to a thermal cycler and run under appropriate conditions (Table 2-4).

Table 2-4: Sequencing reaction thermal cycler conditions.

Stage	**Temperature (°C)**	**Time**
Taq activation	95	1 minute

Denaturation	x25 cycles	95	10 seconds
Annealing		55	5 seconds
Extension		60	4 minutes
Holding		4	∞

Sequencing reaction thermal cycler conditions of the *penA* sequencing assy.

2.8.2.3 Clean-up of sequencing products

A solution of 4% sodium acetate (v/v) buffer in ethanol was prepared by adding 1.6 µL of sodium acetate buffer (Sigma-Aldrich, UK) to 38.4 µL of molecular grade absolute ethanol (Sigma-Aldrich, UK) per active well of the sequencing plate. The plate was sealed with a foil lid (Beckman Coulter, IN, USA), gently vortexed and centrifuged at 2000 g for 20 minutes. The seal was removed, and the plate was inverted onto tissue. The plate was then centrifuged (plate wells facing upwards) at 150 g for one minute to remove excess moisture. Two hundred microlitres of 70% v/v ethanol was added to each well and both centrifugation cycles were repeated. Fifteen microlitres of Hidi formamide (Thermo Fisher Scientific, MA, USA) was added to each well.

2.8.2.4 Sequencing and analysis

Plates of cleaned up sequencing products/HiDi formamide were loaded onto an ABI 3130xl genetic analyser and underwent capillary electrophoresis with POP-7 polymer separation matrix (Thermo Fisher Scientific, MA, USA). Electropherogram traces for each primer were saved as AB1 files and imported into Sequencher. For each sample, traces for each primer were assembled into a contig using the 'assemble automatically' option. The start and stop codon of the gene were located and all upstream/downstream sequence was deleted from the contig. Electropherograms were visually inspected for any erroneous base calls/gaps. The final consensus sequence was exported and queried on the PubMLST *Neisseria* database (section 2.7.5) and unassigned alleles were submitted (section 2.7.6).

2.9 Phylogenetic analyses

2.9.1 Core genome comparisons

Genomes were compared in terms of 1605 core genes (*N. meningitidis* cgMLST c1.0) using the PubMLST genome comparator tool (Bratcher et al., 2014).

2.9.1.1 Refining genome comparator tool variable loci output

Where two allele IDs were present for a single locus, the DNA sequences of both alleles were aligned in BioEdit (section 2.7.4) and compared to determine if genuine differences between the sequences existed. Where they did not, e.g. where the two alleles comprised a single allele and a fragment thereof, the comparison was repeated excluding the affected locus. Where genuine differences did exist, a BLAST search of the sequences was performed against a complete circular genome e.g. MC58 (section 2.7.2) to identify potential paralogues/pseudogenes that may give erroneous results in the comparator. Comparisons were then rerun excluding the affected loci.

2.9.2 Neighbor-Net phylogenetic networks

Following core genome comparisons (section 2.9.1), the resulting distance matrices were exported in Nexus format and imported into SplitsTree4 (version 4.13.1) for visualisation as Neighbor-Net networks (Huson, 1998).

2.9.3 Neighbor joining trees

Multiple nucleotide/amino acid alignments (section 2.7.4) were imported into MEGA4 (Tamura et al., 2007) and a phylogenetic tree was generated by using the neighbor-joining method and the 'number of differences' model. The tree was annotated by adding labels to the alleles of interest. In order to annotate clades by species, the distribution of the

respective alleles was determined by using the ‘search’ and ‘allele designations/scheme fields’ functions on the PubMLST *Neisseria* database.

3 Results

3.1 Antibiotic resistance among *N. meningitidis* isolates in England, Wales and Northern Ireland (2010/11-2018/19)

Objective: To review ABR among IMD isolates received at the MRU from epidemiological years 2010/11-2018/19.

3.1.1 Serogroup and clonal complex distribution

From July 2010 – June 2019, 4,122 IMD isolates received at the MRU from culture-confirmed cases whose genomes were available and downloaded from MGL (accessed 29/06/2020; Appendix 1). Out of the 4,122 isolates, 53% (n=2,178) were serogroup B, 24% (n=1,004) were serogroup W, 16% were serogroup Y (n=651) and 6% were serogroup C (n=237). The remaining isolates (1%) were NG (n=34), serogroup W/Y (n=11), serogroup E (n=4), serogroup X (n=2) and serogroup A (n=1).

The majority of IMD isolates received at the MRU from 2010/11-2018/19 (n=3,449; 84%) belonged to eight main clonal complexes (ST-11 CC, n=1,101; ST-41/44 CC, n=719; ST-23 CC, n=549; ST-269 CC, n=507; ST-213 CC, n=238; ST-32 CC, n=184; ST-461 CC, n=76 and ST-22 CC, n=75). The remaining isolates belonged to less prevalent CCs (n=290), were unassigned to a CC (n=233) or had incomplete MLST profiles (n=150).

3.1.2 Penicillin susceptibility

3.1.2.1 MIC distribution

Of the 4,122 IMD isolates, 63% (n=2,591) were penicillin-susceptible, standard exposure (PenS; MICs 0.004-0.064 mg/L), 34% (n=1,418) were penicillin-susceptible, increased exposure (PenI; MICs 0.094-0.25 mg/L) and 3% (n=113) were penicillin-resistant (PenR; MICs 0.38-0.75 mg/L). The lowest proportion of PenS isolates were received in

epidemiological years 2015/16 and 2018/19 (52%) and the highest proportion of PenR isolates were received in 2018/19 (7%) (Table 3-1).

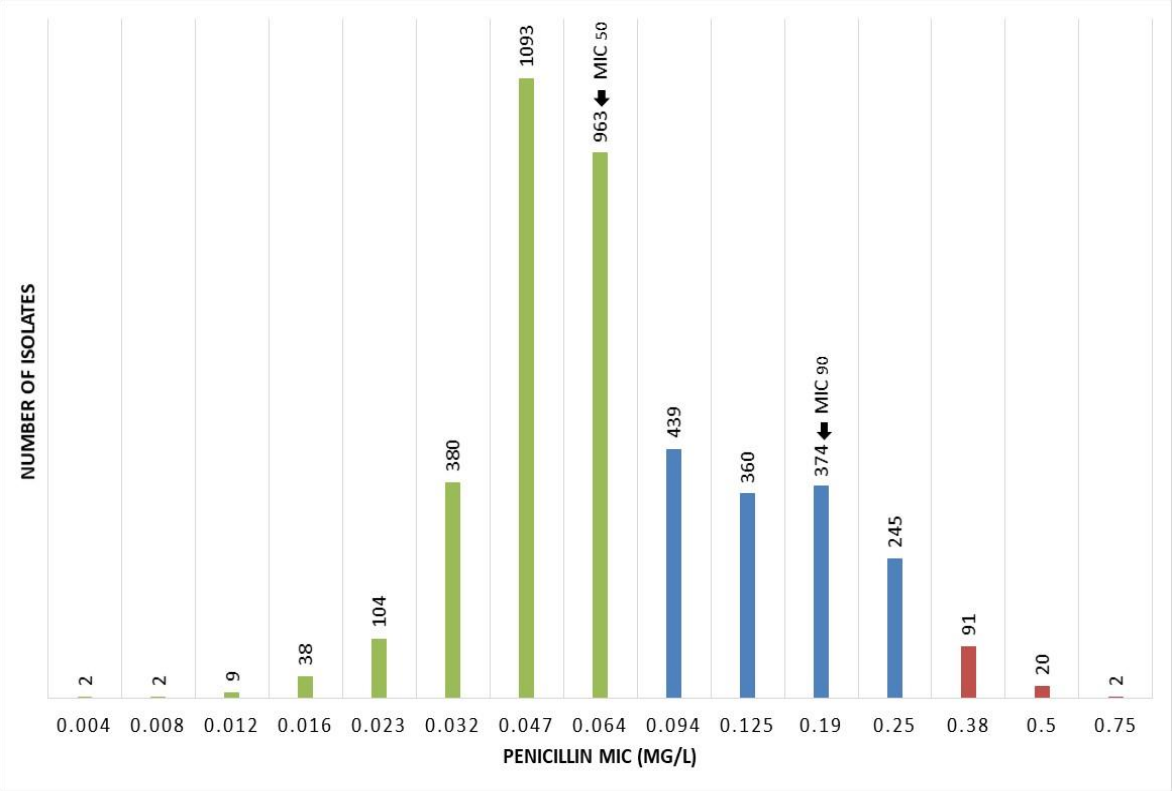
Table 3-1: Distribution of penicillin susceptibility among IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.

	Number of IMD isolates (%)									
	2010/11 (n=500)	**2011/12 (n=400)**	**2012/13 (n=450)**	**2013/14 (n=403)**	**2014/15 (n=505)**	**2015/16 (n=521)**	**2016/17 (n=501)**	**2017/18 (n=488)**	**2018/19 (n=354)**	**Total (n=4,122)**
PenS ≤0.06 mg/L	336 (67.20)	277 (69.25)	277 (61.56)	247 (61.29)	349 (69.11)	272 (52.21)	335 (66.87)	313 (64.14)	185 (52.26)	2,591 (62.86)
PenI 0.094-0.25 mg/L	157 (31.40)	123 (30.75)	164 (36.44)	148 (36.72)	150 (29.70)	223 (42.80)	150 (29.94)	159 (32.58)	144 (40.86)	1,418 (34.40)
PenR >0.25 mg/L	7 (1.40)	0 (0.00)	9 (2.00)	8 (1.99)	6 (1.19)	26 (4.99)	16 (3.19)	16 (3.28)	25 (7.06)	113 (2.74)

PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines. The annual percentage of PenS, I and R isolates is also displayed.

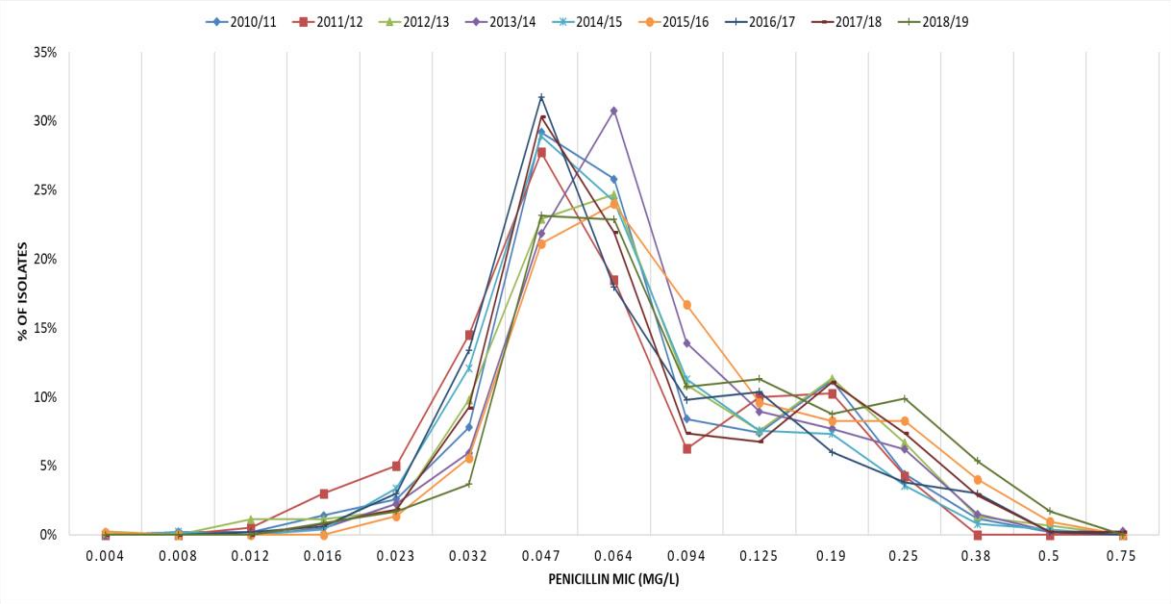
Penicillin MIC values of all IMD isolates ranged from 0.004 - 0.75 mg/L (Figure 3-1). Isolates with MICs of 0.047 mg/L were most common (n= 1,093; 27%). The MIC_{50} and the MIC_{90}, defined as the lowest concentration of the antibiotic required to inhibit the growth of 50% and 90% of organisms, respectively, were 0.064 mg/L and 0.19 mg/L, respectively. In 2018/19, the highest proportion of isolates with MICs of 0.125-0.38 mg/L were observed (Figure 3-2).

Figure 3-1: Penicillin MICs among invasive meningococcal disease isolates in England, Wales and Northern Ireland from 2010/11-2018/19.



The green bars represent PenS isolates, blue bars represent PenI isolates and red bars represent PenR isolates. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines. The MIC_{50} and MIC_{90} are also indicated.

Figure 3-2: Annual proportion of penicillin MICs among IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.



Percentage of IMD isolates with each MIC value per epidemiological year (2010/11; n=500, 2011/12; n=400, 2012/13; n=450, 2013/14; n=403, 2014/15; n=505, 2015/16; n=521, 2016/17; n=501, 2017/18; n=488, 2019/19; n=354).

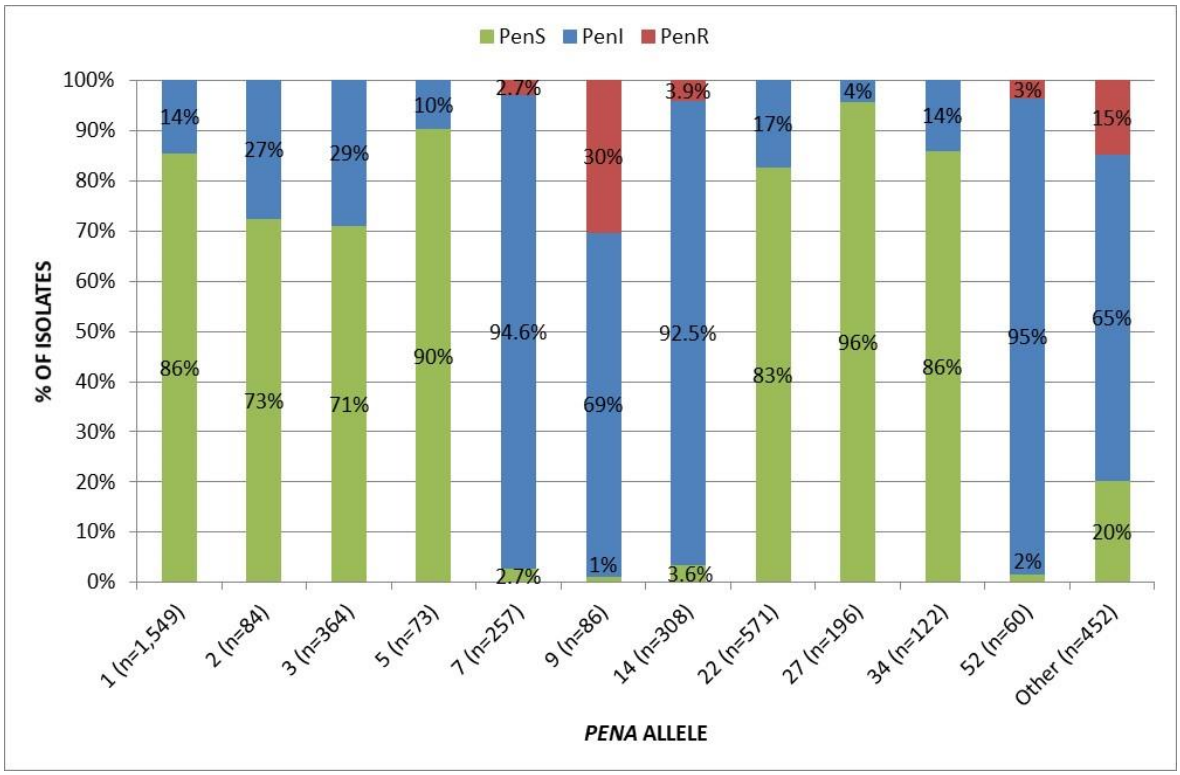
3.1.2.2 *PenA* allele distribution

The 402 bp *penA* fragment of the NEIS1753 PBP2 gene, corresponding to AA residues 441-575, was obtained for the 4,122 IMD isolates received at the MRU from 2010/11-2018/19. One hundred and thirty-three *penA* alleles were identified, with frequencies of isolates harbouring these alleles varying from 1 to 1,549. The most prevalent *penA* alleles (*penA1*, *penA2*, *penA3*, *penA5*, *penA7*, *penA9*, *penA14*, *penA22*, *penA27*, *penA34* and *penA52*) found among 89% of isolates, are displayed in Figure 3-3 with the corresponding distribution of penicillin susceptibility. *PenA1* was the most prevalent (n=1,549; 38%) followed by *penA22* (n=571; 14%). Isolates harbouring *penA1* and *penA22* were PenS (86% and 83%, respectively) and PenI (14% and 17%, respectively). Among the most prevalent alleles, the highest proportion of PenR isolates were those with *PenA9*, where 30% of isolates with *penA9* were PenR. *PenA* alleles 7, 14 and 52 were also found among PenR isolates. The

highest proportion of PenI isolates were those with *PenA7* and *penA52* (95%) followed by those with *penA14* (93%).

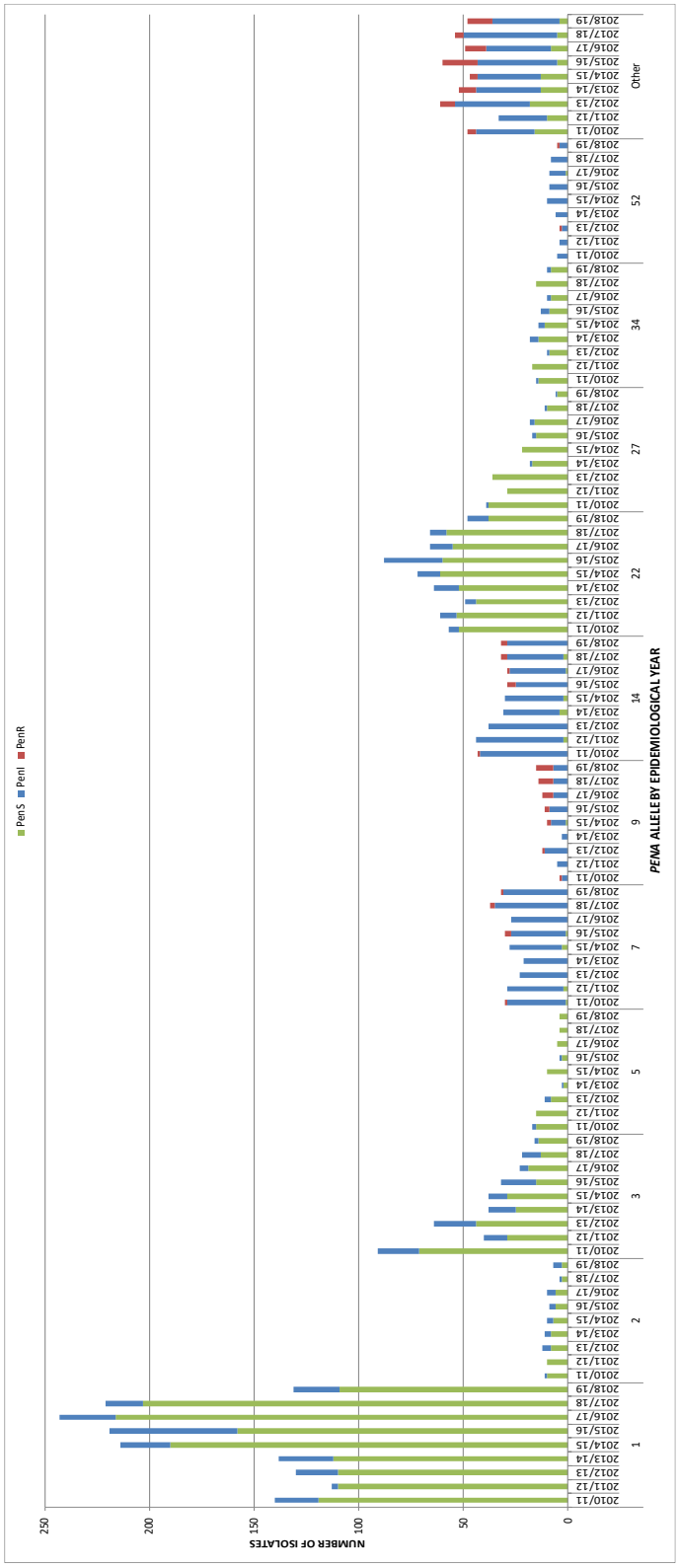
Isolates harbouring *penA1* increased in number from 2011/12 to 2016/17, decreasing in subsequent years (Figure 3-4). A decrease in the number of isolates harbouring *penA3* and *penA27*, mainly associated with PenS isolates, was observed over time. The number of isolates harbouring *penA7*, *penA14* and *penA52* (associated with mainly PenI isolates), remained stable annually.

Figure 3-3: Penicillin susceptibility among IMD isolates with the most prevalent *penA* alleles in England, Wales and Northern Ireland from 2010/11-2018/19.



PenA alleles observed among n=4,122 IMD isolates. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

Figure 3-4: *PenA* alleles among IMD isolates in England, Wales and Northern Ireland and the distribution of penicillin susceptibility from 2010/11-2018/19.



P*enA* alleles among n=4,122 IMD isolates. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

Thirty-one *penA* alleles were identified among the 133 PenR IMD isolates. These are listed in Table 3-2, along with other *penA* alleles (n=19) identified among PenI isolates represented by four or more isolates. The geometric mean MIC, MIC_{50} and MIC_{90} of penicillin were determined for the isolates with each of these alleles. Twenty-eight out of the 31 *penA* alleles among the PenR IMD isolates harboured all five of the AASs associated with conferring reduced susceptibility or resistance to penicillin (F504L, A510V, I515V, H541N, and I566V; Appendix 4). Three *penA* alleles (*penA*171, *penA*209, and *penA*327) did not have all five of these AASs. *PenA327* contained four (F504L, A510V, I515V, H541N), *penA209* contained three (F504L, A510V, I515V) whilst *penA171* contained none. Further analyses of these alleles and representative isolates were performed (sections 3.1.2.5-7).

Table 3-2: *PenA* alleles among PenR and PenI IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.

penA allele	Number of isolates	Number of PenS isolates	Number of PenI isolates	Number of PenR isolates	MIC value or range (mg/mL)	MIC50 (mg/mL)	MIC90 (mg/mL)	Number of resistance-associated amino acid alterations
1	1549	1327	222	0	0.004-0.25	0.047	0.094	0
2	84	61	23	0	0.016-0.25	0.064	0.125	0
3	364	259	105	0	0.047-0.25	0.064	0.094	0
4	13	11	2	0	0.016-0.094	0.047	0.094	0
5	73	66	7	0	0.012-0.19	0.047	0.064	0
7	257	7	243	7	0.064-0.38	0.190	0.250	5
9	86	1	59	26	0.047-0.75	0.250	0.380	5
10	5	0	2	3	0.25-0.38			5
11	1	0	0	1	0.5			5
12	16	0	14	2	0.125-0.5	0.190	0.380	5
13	7	0	5	2	0.125-0.38			5
14	308	11	285	12	0.047-0.5	0.190	0.250	5
16	9	8	1	0	0.023-0.094			0
19	22	1	18	3	0.047-0.38	0.190	0.380	5
20	6	0	5	1	0.125-0.5			5
21	3	0	1	2	0.19-0.38			5
22	571	473	98	0	0.012-0.19	0.064	0.094	0
25	3	0	2	1	0.125-0.38			5
27	196	188	8	0	0.008-0.125	0.047	0.064	0
33	43	0	27	16	0.094-0.75	0.250	0.500	5
34	122	105	17	0	0.012-0.19	0.047	0.094	0
42	11	0	10	1	0.125-0.38	0.190	0.250	5
52	60	1	57	2	0.064-0.38	0.190	0.250	5
54	1	0	0	1	0.38			5
62	5	3	2	0	0.032-0.094			0
66	5	0	5	0	0.094-0.25			5
83	4	2	2	0	0.047-0.125			0
90	5	0	5	0	0.125-0.19			5
91	4	0	4	0	0.125-0.19			5
110	2	0	1	1	0.125-0.38			5
119	4	1	3	0	0.032-0.125			0
157	15	14	1	0	0.032-0.094	0.047	0.064	0
171	1	0	0	1	0.38			0
179	1	0	0	1	0.38			5
209	1	0	0	1	0.5			3
238	5	0	5	0	0.094-0.19			5
248	46	1	35	10	0.047-0.38	0.250	0.380	5
295	6	0	3	3	0.25-0.5			5
327	5	1	3	1	0.047-0.38			4
331	1	0	0	1	0.5			5
342	4	2	2	0	0.047-0.094			0
348	16	2	11	3	0.047-0.38	0.125	0.380	5
371	5	0	4	1	0.125-0.38			5
386	10	1	9	0	0.047-0.125	0.125	0.125	5
414	8	0	7	1	0.125-0.38			5
419	1	0	0	1	0.5			5
420	8	0	8	0	0.125-0.25			5
435	1	0	0	1	0.38			5
540	6	0	1	5	0.25-0.38			5
593	1	0	0	1	0.38			5
921	1	0	0	1	0.38			5

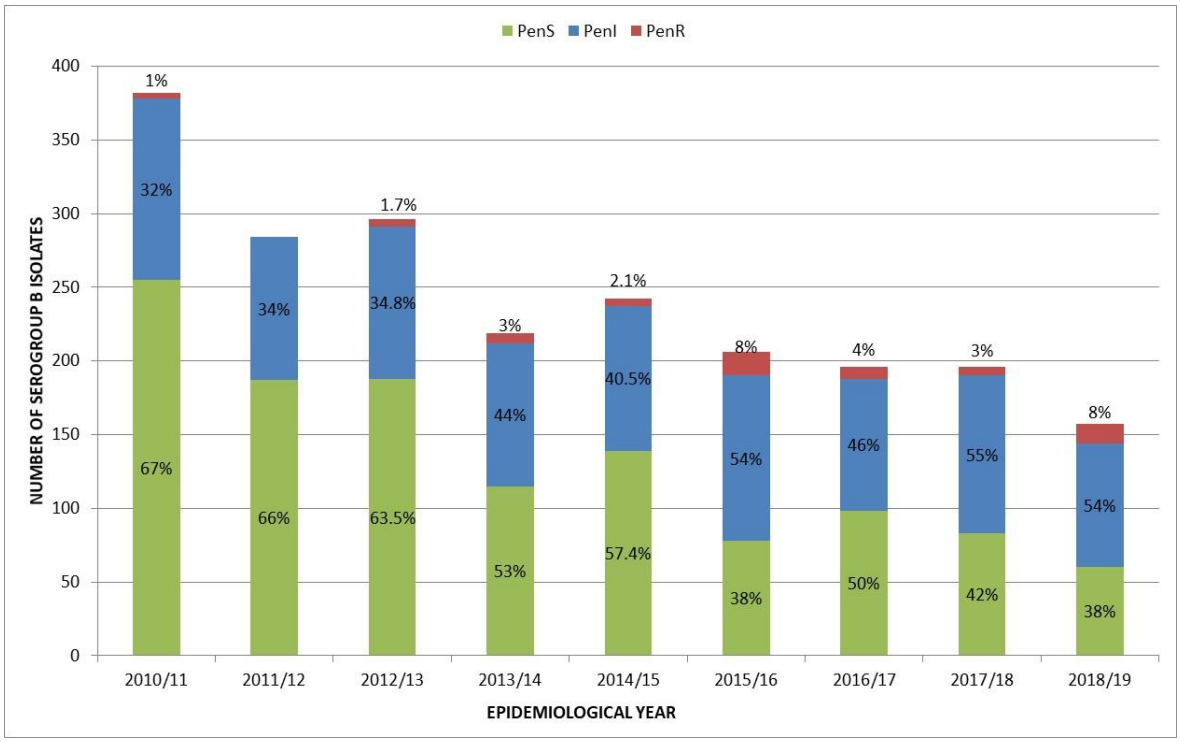
Alleles among n=3,981 IMD isolates. Alleles among PenI IMD isolates represented by 4+ isolates only. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines. MIC_{50} and MIC_{90} calculated for ≥10 isolates.

3.1.2.3 Serogroup distribution

3.1.2.3.1 Serogroup B

Serogroup B IMD isolates (n=2,178) were PenS (n=1203; 55%), PenI (n=911; 42%) and PenR (n=64; 3%). The number of serogroup B isolates decreased over the time period, from the highest in 2010/11 (n=382) to the lowest in 2018/19 (n=157) (Figure 3-5). As the number of serogroup B isolates decreased, so did the proportion of serogroup B PenS isolates, from 67% in 2010/11 to 38% in 2018/19. The number and proportion of PenI isolates has increased gradually over time from 32% in 2010/11 to 54-55% in 2017/18 - 2018/19. The highest annual proportions of serogroup B PenR isolates were in 2015/16 (8%) and 2018/19 (8%).

Figure 3-5: Annual distribution of penicillin susceptiblity among serogroup B IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.

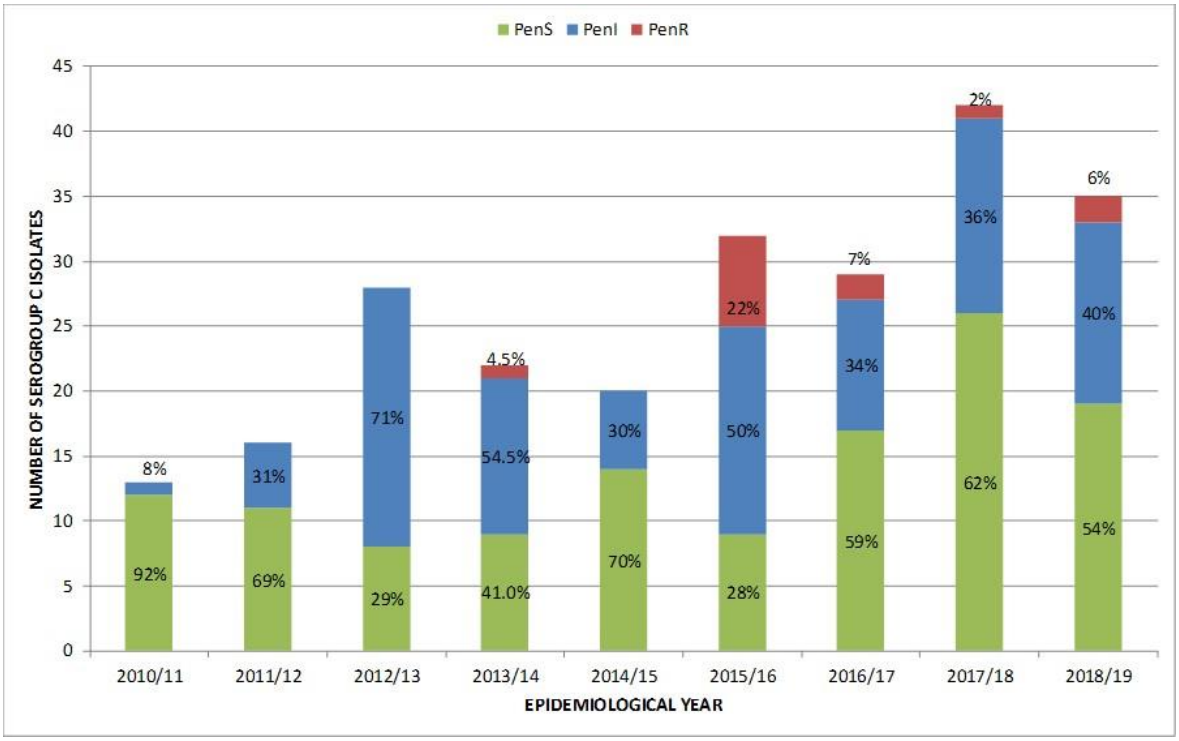


n=2,178 serogroup B isolates. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

3.1.2.3.2 Serogroup C

Serogroup C IMD isolates (n=237) were PenS (n=125; 53%), PenI (n=99; 42%) and PenR (n=13; 5%). Overall, an increase was observed in the number of serogroup C isolates over the time period, from 13 in 2010/11 to 35 in 2018/19 (Figure 3-6). The highest proportion of serogroup C PenS isolates was observed in 2010/11 (92%) and the lowest was observed in 2015/16 (28%). The highest annual proportion of PenI (50%) and PenR isolates (22 %) was observed in 2015/16. The distribution of PenS, PenI and PenR serogroup C isolates varied year by year.

Figure 3-6: Annual distribution of penicillin susceptibility among serogroup C IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.

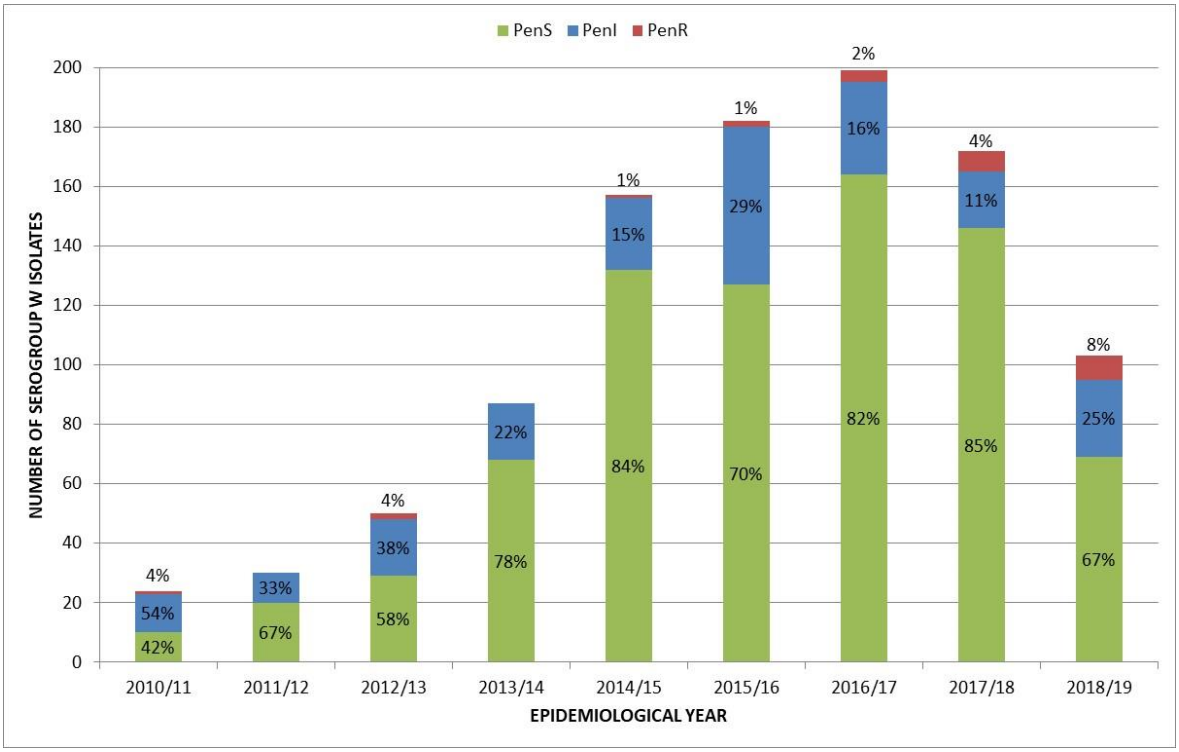


n=237 serogroup C isolates. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

3.1.2.3.3 Serogroup W

Serogroup W IMD isolates (n=1,004) were PenS (n=765; 76%), PenI (n=214; 21%) and PenR (n=25; 3%). The number of serogroup W isolates increased annually from 2010/11 (n=24), peaked in 2016/17 (n=199) and fell annually to 2018/19 (n=103) (Figure 3-7). Overall, as the number of serogroup W isolates increased over time, so did the number and proportion of serogroup W PenS isolates. An annual increase in the proportion of PenR serogroup W isolates from 2015/16 (1%) to 2018/19 (8%) was observed.

Figure 3-7: Annual distribution of penicillin susceptibility among serogroup W IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.

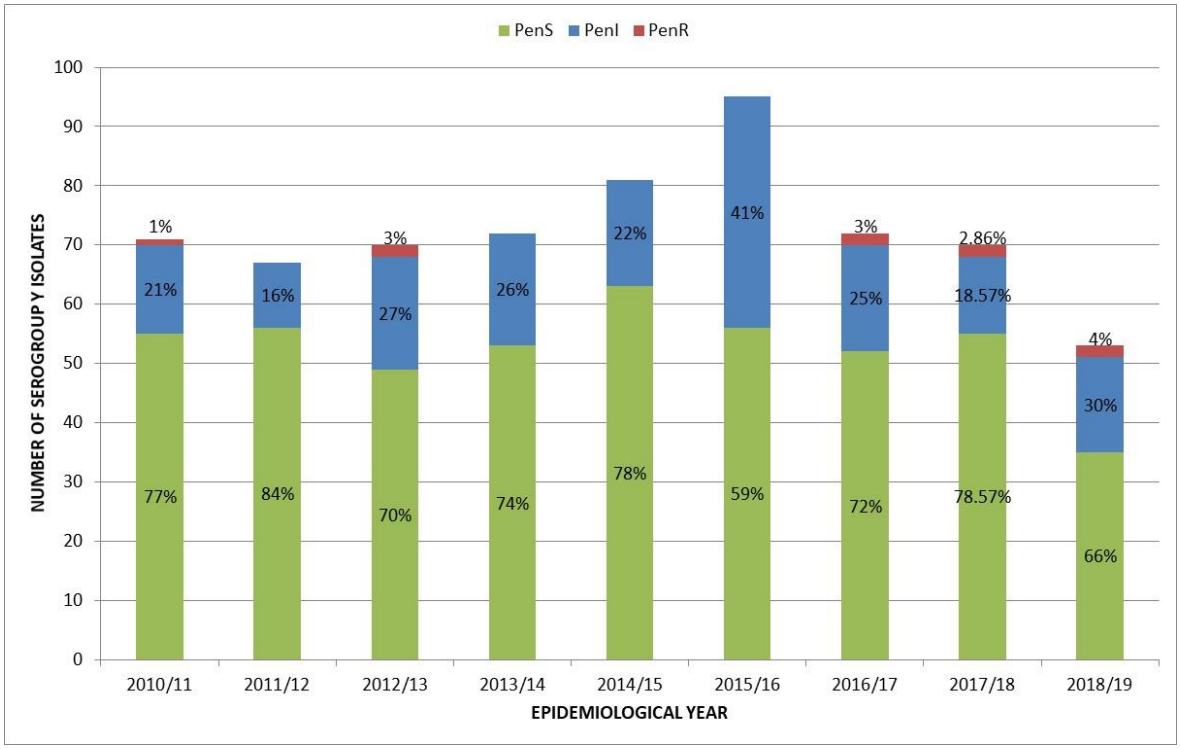


n=1,004 serogroup W IMD isolates. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

3.1.2.3.4 Serogroup Y

Six hundred and fifty-one serogroup Y isolates were received from 2010/11-2018/9 (16%). Seventy-three percent (n=474) were PenS, 26% were PenI (n=168) and 1% were PenR (n=9). The annual number of serogroup Y isolates remained relatively stable over the time period, as did the number and proportion of PenS isolates (Figure 3-8). The highest proportion of PenI serogroup Y isolates (41%) was in 2015/16. In 2018/19, the highest proportion of serogroup Y PenR isolates was observed (4%).

Figure 3-8: Annual distribution of penicillin susceptibly among serogroup Y IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.



n=651 serogroup Y IMD isolates. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

3.1.2.3.5 Serogroup distribution among the penicillin-resistant IMD isolates

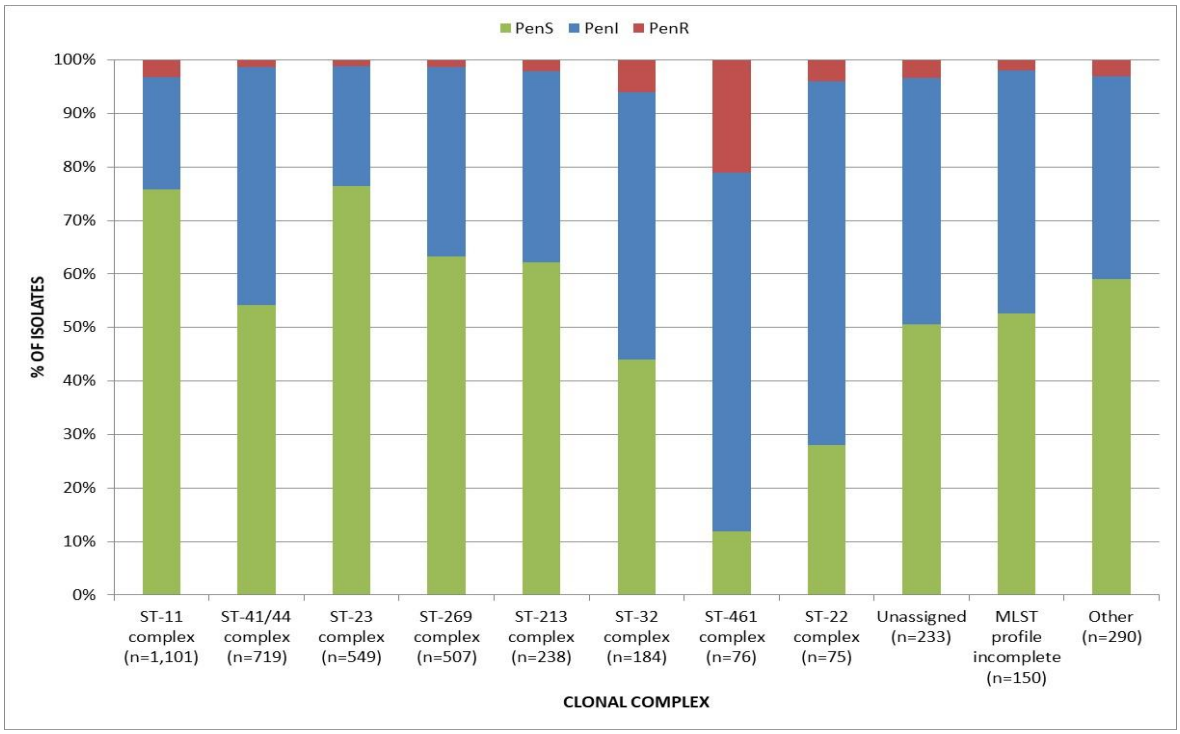
Out of the 113 PenR isolates received at the MRU from 2010/11-2018/19, 64 were serogroup B, 25 were serogroup W, 13 were serogroup C, nine were serogroup Y, one was serogroup W/Y and one was NG.

3.1.2.4 Clonal Complex distribution

3.1.2.4.1 Overview

The most prevalent CC was the ST-11 CC (n=1,101, 27%) followed by the ST-41/44 CC (n=720, 17%) (Figure 3-9). The proportion of PenS isolates among these two CCs were 76% and 54%, respectively. The ST-461 CC had the highest proportion of PenR isolates (21%) and had the lowest proportion of PenS isolates (12%). All PenR ST-461 CC isolates harboured *penA33* as did 47% of PenI ST-461 CC isolates. The CC with the second highest proportion of PenR isolates was ST-32 CC isolates (6%).

Figure 3-9: Distribution of penicillin susceptibility among IMD isolates in the most prevalent clonal complexes in England, Wales and Northern Ireland from 2010/11-2018/19.



Clonal complexes of n=4,122 IMD isolates and distribution of PenS, I and R isolates. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

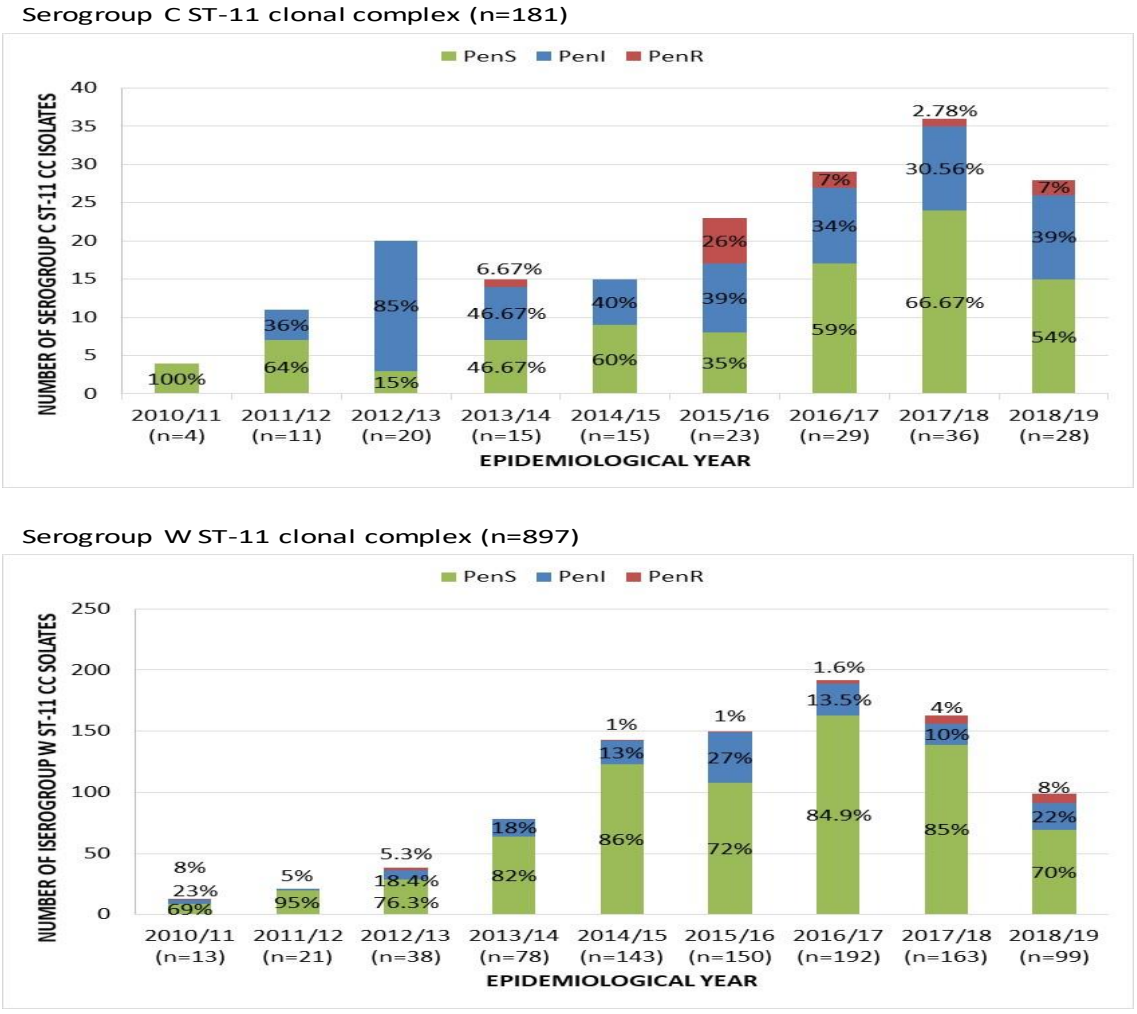
3.1.2.4.2 Among the penicillin-resistant IMD isolates

Out of the 113 PenR isolates received at the MRU from 2010/11–2018/19, 36 belonged to ST-11 CC, 16 belonged to ST-461 CC, 11 belonged to ST-32 CC, nine belonged to ST-41/44 CC, seven belonged to ST-269 CC, six belonged to ST-23 CC, five belonged to ST-213 CC, four belonged to ST-162 CC, three belonged to ST-22 CC, two belonged to ST-53 CC and one belonged to ST-4821 CC, ST-174 CC and ST-167 CC. Eight PenR isolates were unassigned to a CC and three had incomplete MLST profiles.

3.1.2.4.3 The ST-11 clonal complex

Ninety-seven percent of ST-11 CC isolates were serogroup W or serogroup C (81% and 16%, respectively). Overall, serogroup C ST-11 CC isolates had greater proportions of PenI and PenR isolates compared with serogroup W ST-11 CC isolates (Figure 3-10). Since 2015/16, the annual proportion of PenR serogroup W ST-11 isolates increased from 1% in 2015/16 to 8% in 2018/19. An investigation into this increase is detailed in section 3.3.

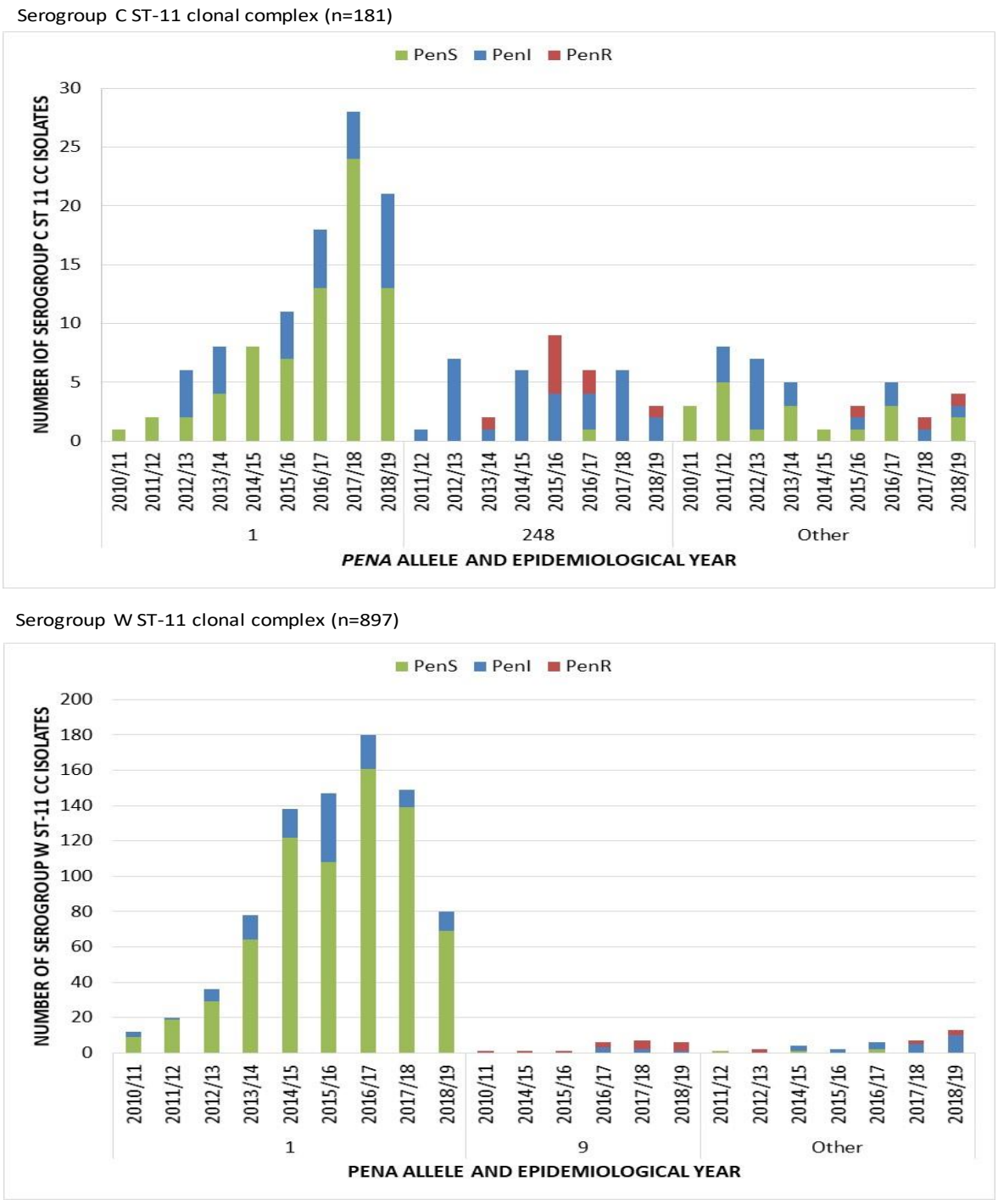
Figure 3-10: Distribution of penicillin susceptibility among Serogroup C and W ST-11 clonal complex IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.



PenS = Penicillin -susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

The most prevalent allele among serogroup C and W ST-11 CC isolates was *penA1* (Figure 3-11), found among 57% of serogroup C ST-11 CC isolates and 94 % of serogroup W ST-11 CC isolates. The number of serogroup C ST-11 CC isolates harbouring *penA1* increased annually from 2010/11, except for in 2018/19. *PenA248* was harboured by 28% of serogroup C ST-11 CC isolates. The annual number of serogroup C ST-11 CC isolates with *penA248* remained relatively stable and was associated mainly with PenI and PenR isolates. The number of serogroup W ST-11 CC isolates harbouring *penA1* increased from 2010/11 before decreasing in 2017/18. *PenA9* was harboured by 3% of serogroup W ST-11 CC isolates. The number of PenR isolates harbouring *penA9* increased over time, from one PenR isolate received in 2010/11 to seven received in 2018/19.

Figure 3-11: Distribution of penicillin susceptibility among serogroup C and W ST-11 clonal compelx IMD isolates with the corresponding most prevalent *penA* alleles in England, Wales and Northern Ireland from 2010/11-2018/19.

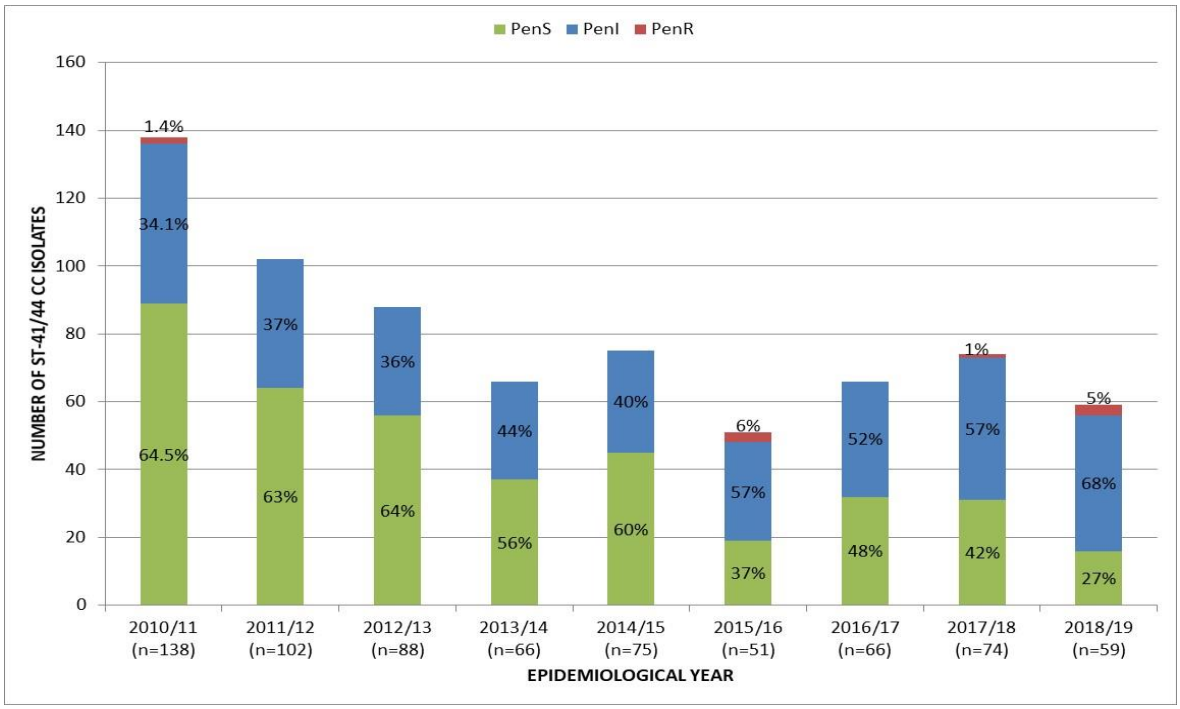


PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

3.1.2.4.4 ST-41/44 clonal complex

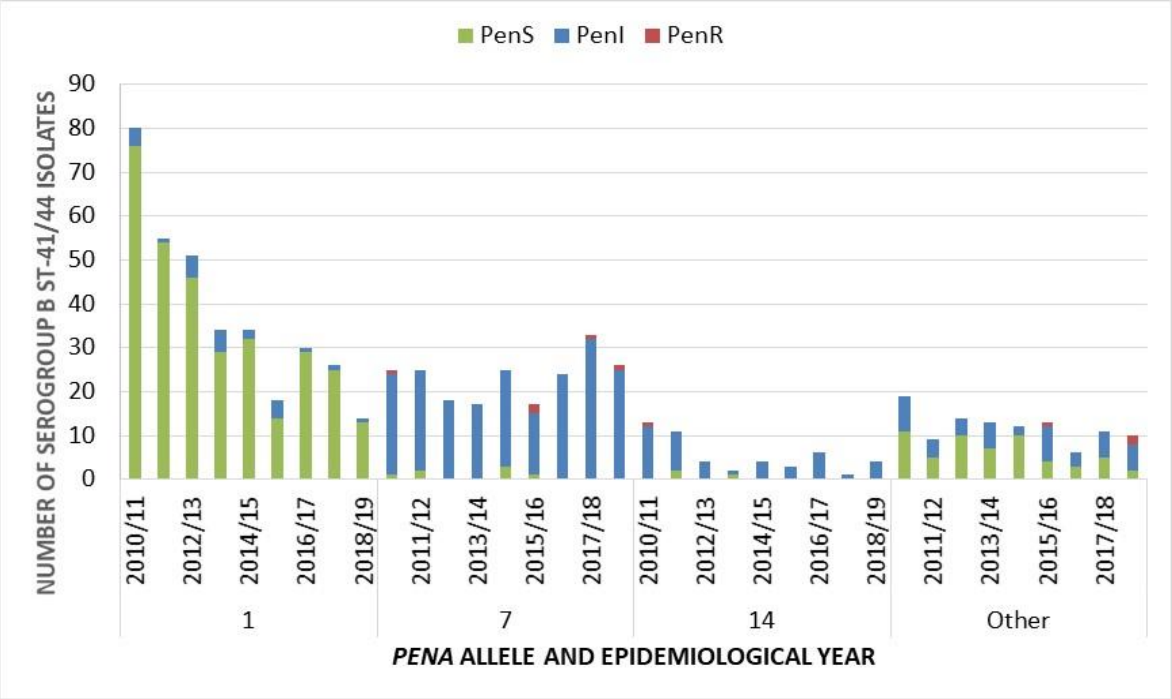
The number of ST-41/44 CC isolates received at the MRU decreased over the time period, from 138 in 2010/11 to 59 in 2018/19 (Figure 3-12). As the number of isolates decreased, so did the number and proportion of PenS ST-41/41 CC isolates. The highest proportion of PenS ST-41/44 CC isolates was in 2010/11 (n=89; 64.5%), the lowest in 2018/19 (n=16, 27%). Most ST-41/44 CC isolates were serogroup B (n=707, 98%). The most prevalent *penA* alleles found among serogroup B ST-41/44 isolates were *penA1* (48%), *penA7* (30%) and *penA14* (7%). Overall, the annual number of serogroup B ST-44/44 CC isolates with *penA1* (mainly PenS) decreased over time whilst isolates with *penA7* and *penA14* (mainly PenI) remained stable (Figure 3-13). The decrease in the number of serogroup B ST-41/44 C isolates with *penA1* over time did not appear to be associated with a particular lineage of this clonal complex (Figure 3-14).

Figure 3-12: Annual distribution of penicillin susceptibility among serogroup B ST-41/44 clonal complex IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.



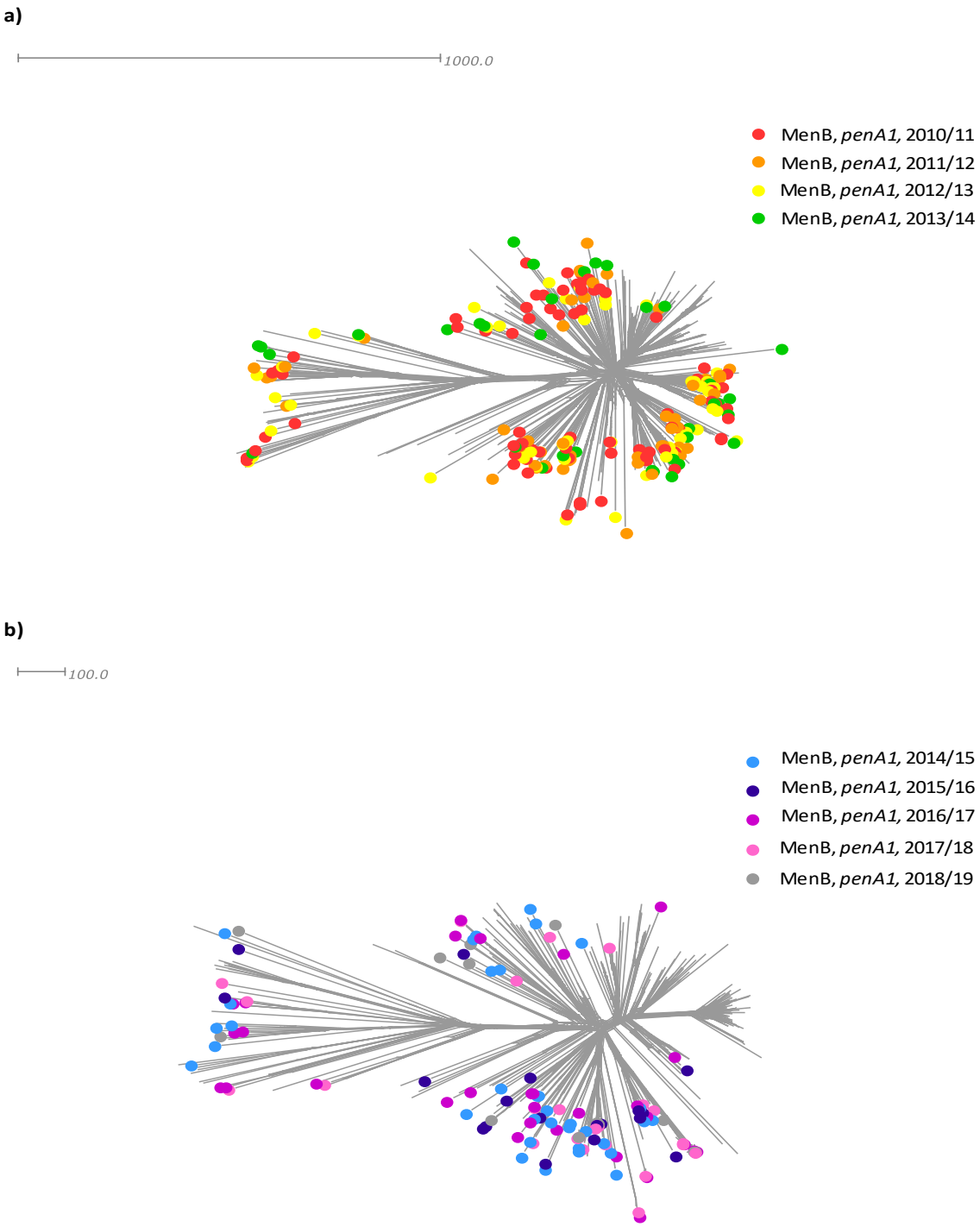
n=719 ST-41/44 CC IMD isolates. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

Figure 3-13: Distribution of penicillin susceptbility among serogroup B ST-41/44 clonal complex isolates with the corresponding most prevalent *penA* alleles in England, Wales and Northern Ireland from 2010/11-2018/19.



n=707 serogroup B ST-41/44 CC IMD isolates. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

Figure 3-14: Annual distribution of serogroup B ST-41/44 CC IMD isolates from E,W and NI harbouring *penA1* among all ST-41/44 CC IMD isolates from E,W and NI 2011/11-2018/19.

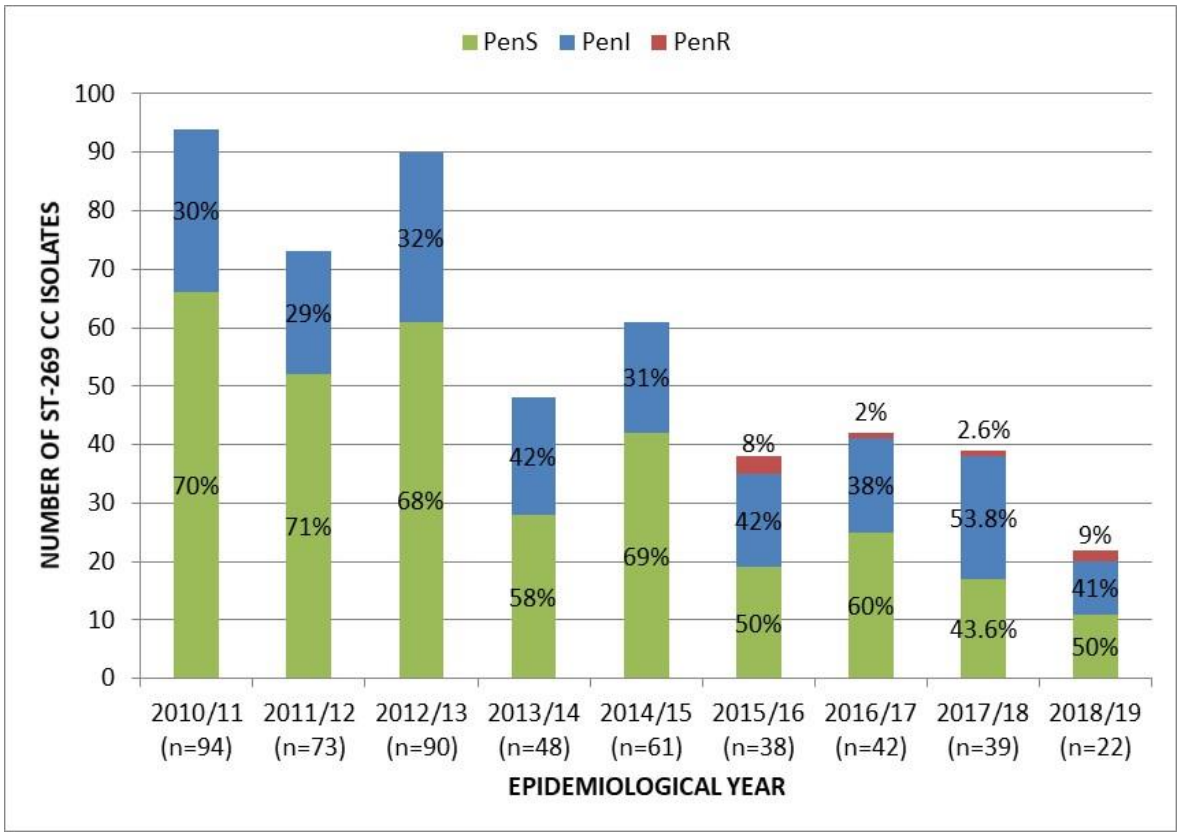


Core genome comparison of 1605 core genome loci among ST 41-44 clonal complex IMD isolates from E, W and NI. Genomes split into two groups: a) = ST-41/44 clonal complex genomes from 2010/11-2013/14 (n=394), b) = ST-41/44 clonal complex genomes from 2014/15-2018/19 (n=325). MenB = meningococcal serogroup B. The number of variable loci among the 1605 that were compared is represented by the scale bar.

3.1.2.4.5 The ST-269 clonal complex

Twelve percent of all IMD isolates received from 2010/11-2018/19 belonged to ST-269 CC (n=507). The number of ST-269 CC isolates decreased over time, along with the number and proportion of PenS ST-269 CC isolates (Figure 3-15). The annual number of PenI ST-269 CC isolates remained relatively stable.

Figure 3-15: Annual distribution of penicillin susceptibility among ST-269 clonal complex IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.



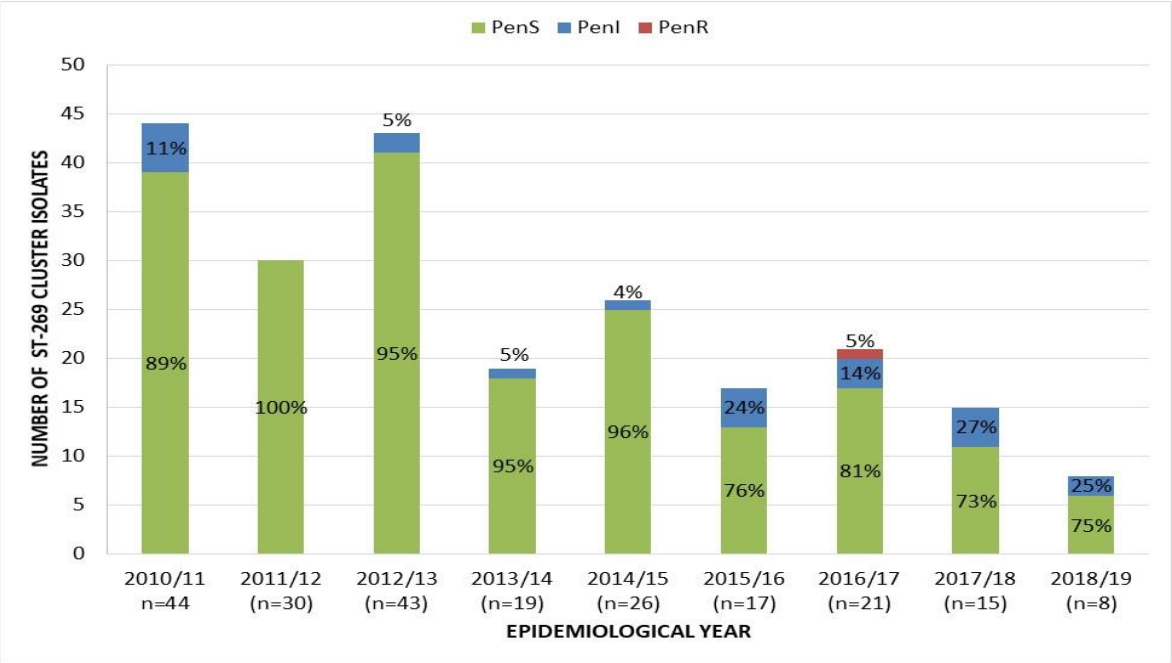
n=507 ST-269 clonal complex IMD isolates. PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

ST-269 CC comprised isolates of two main clusters: ST-269 and ST-275 clusters (Appendix 5). Fifty-five percent of ST-269 CC isolates belonged to the ST-275 cluster (n=279) and 44% belonged to the ST-269 cluster (n=223). One percent of ST-269 CC isolates did not fall into either cluster. PenS isolates in both clusters decreased annually (Figure 3-16). The ST-269 cluster comprised mainly PenS isolates, whilst PenI isolates were more prevalent among the ST-275 cluster. Most ST-269 CC isolates were serogroup B, comprising 96% and 99% of ST-269 and ST-275 cluster isolates, respectively. *PenA27* was the most prevalent among serogroup B ST-269 cluster isolates, harboured by 85% of isolates. An overall decrease of serogroup B ST-269 cluster isolates with *penA27* was observed over time (Figure 3-17). *PenA3* and *penA14* were the most prevalent alleles among serogroup B ST-275 cluster isolates, harboured by 57% and 30% of isolates, respectively. A decrease was observed in PenS ST-275 cluster isolates with *penA3* over the time. Overall, the annual number of PenI ST-275 cluster isolates with *penA14* remained relatively stable.

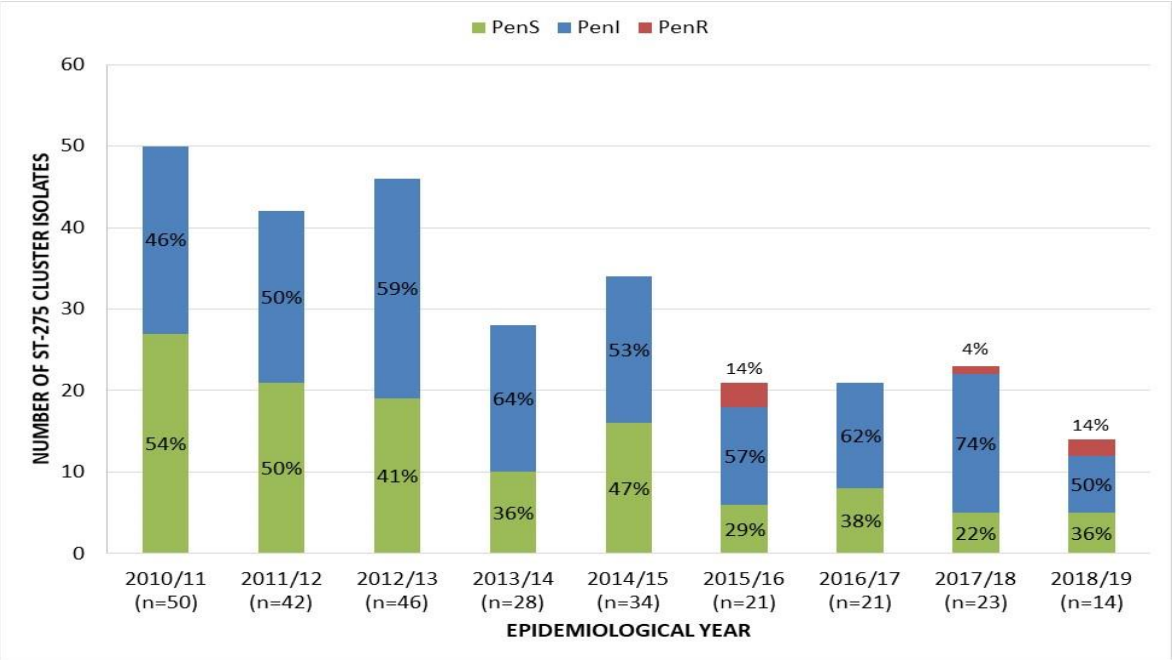
The decrease over time in the number of serogroup B ST-269 cluster isolates with *penA27* and the number of serogroup B ST-275 cluster isolates with *penA3* did not appear to be associated with particular lineages of these clusters (Figure 3-18).

Figure 3-16: Annual distribution of penicillin susceptibility among ST-269 and ST-275 cluster isolates of ST-269 clonal complex in England, Wales and Northern Ireland from 2010/11-2018/19.

ST-269 cluster isolates (n=223)



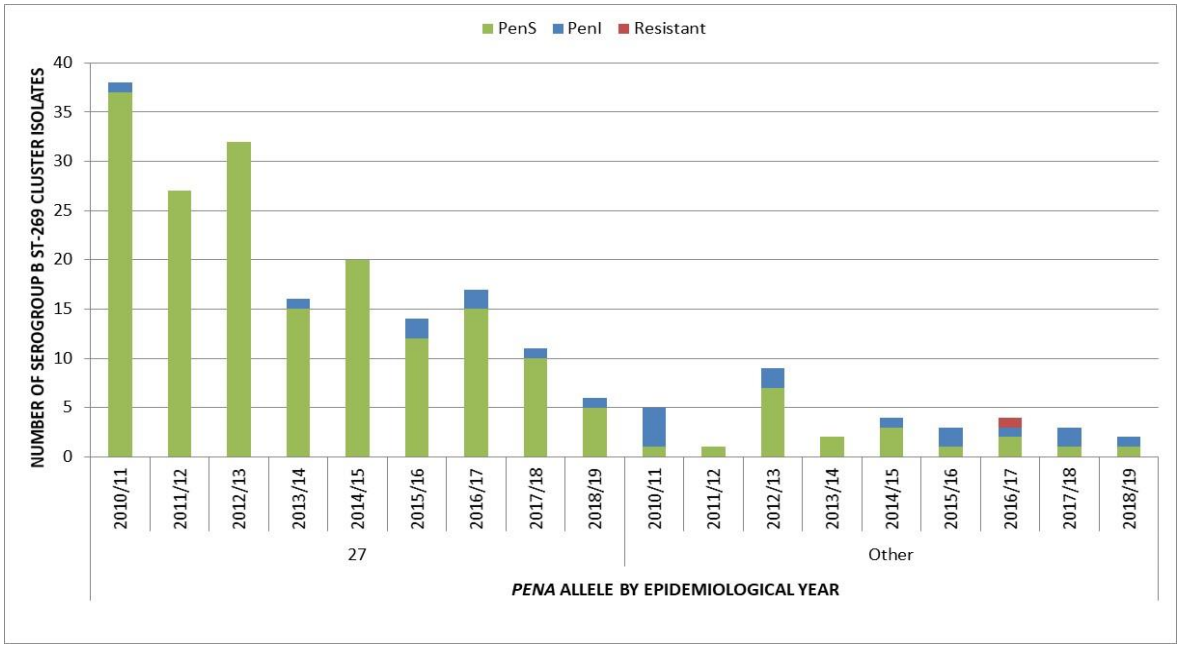
ST-275 cluster isolates (n=279)



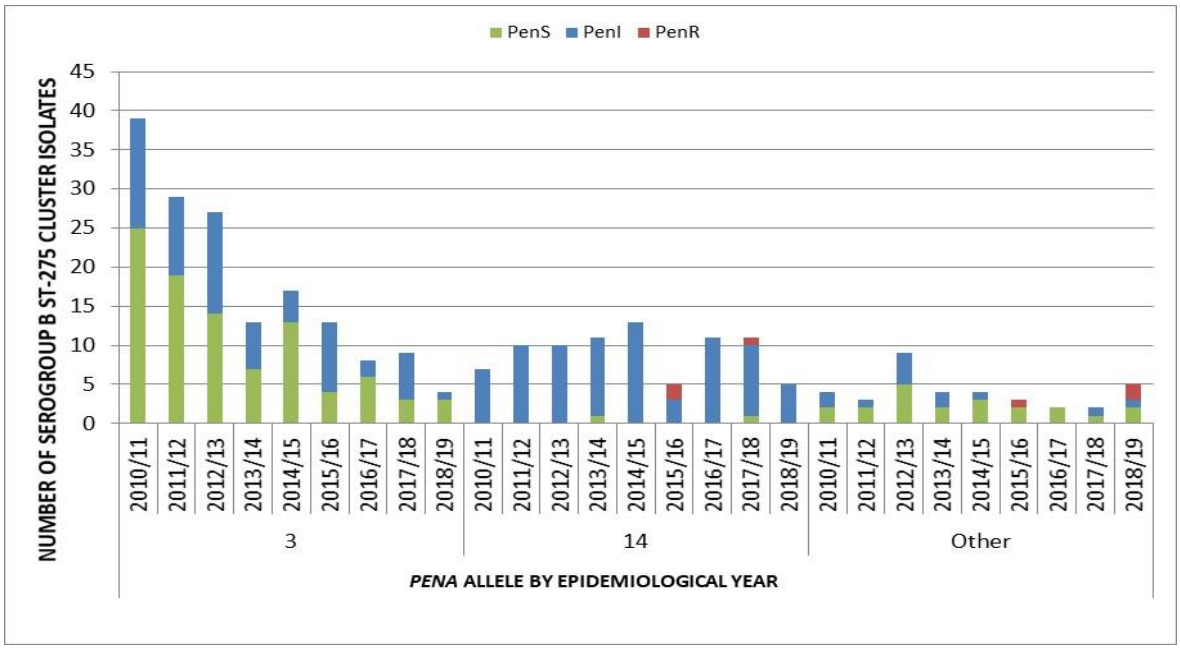
PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

Figure 3-17: Distribution of penicillin susceptibility among serogroup B ST-269 and ST-275 cluster isolates of ST-269 clonal complex with the corresponding most prevalent *penA* alleles in England, Wales and Northern Ireland from 2010/11-2018/19.

Serogroup B ST-269 cluster isolates (n=214)

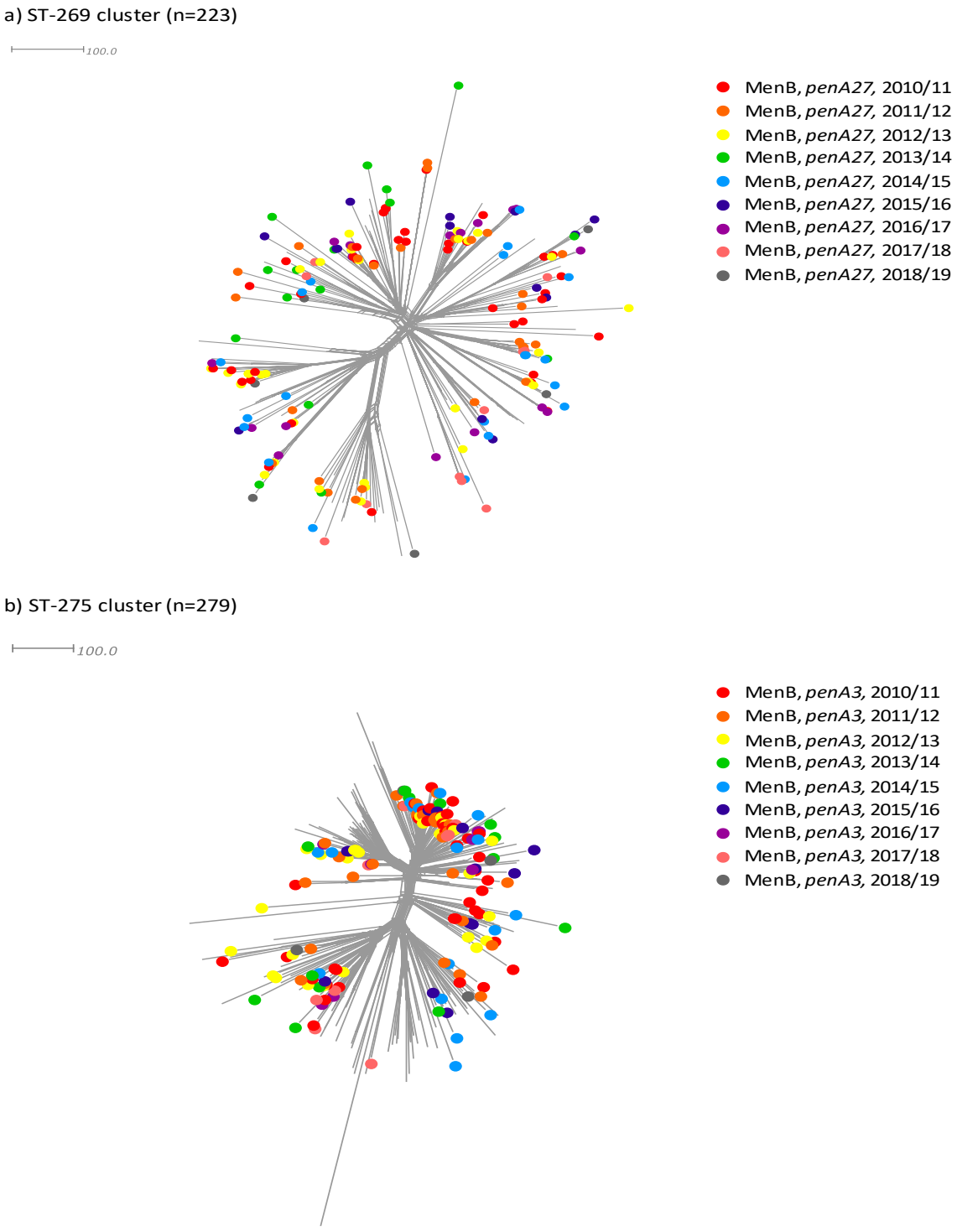


Serogroup B ST-275 cluster isolates (n=278)



PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

Figure 3-18: Annual distribution of serogroup B ST-269 and ST-275 cluster IMD isolates from E,W and NI 2011/11-2018/19 harbouring *penA27* and *penA3*, respectively.

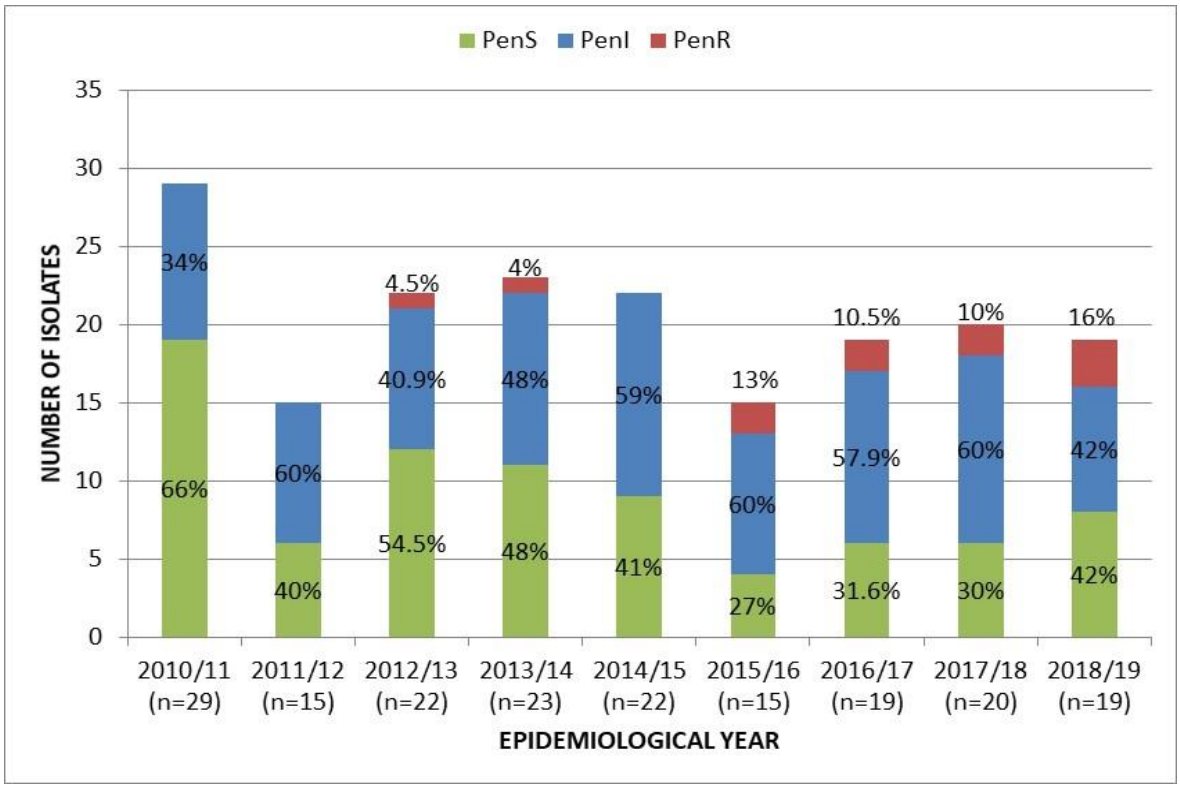


Core genome comparisons of 1605 core genome loci among ST 269 cluster (a) and ST-275 cluster (b) IMD isolates from E, W and NI. MenB = meningococcal serogroup B. The number of variable loci among the 1605 that were compared is represented by the scale bars.

3.1.2.4.6 The ST-32 clonal complex

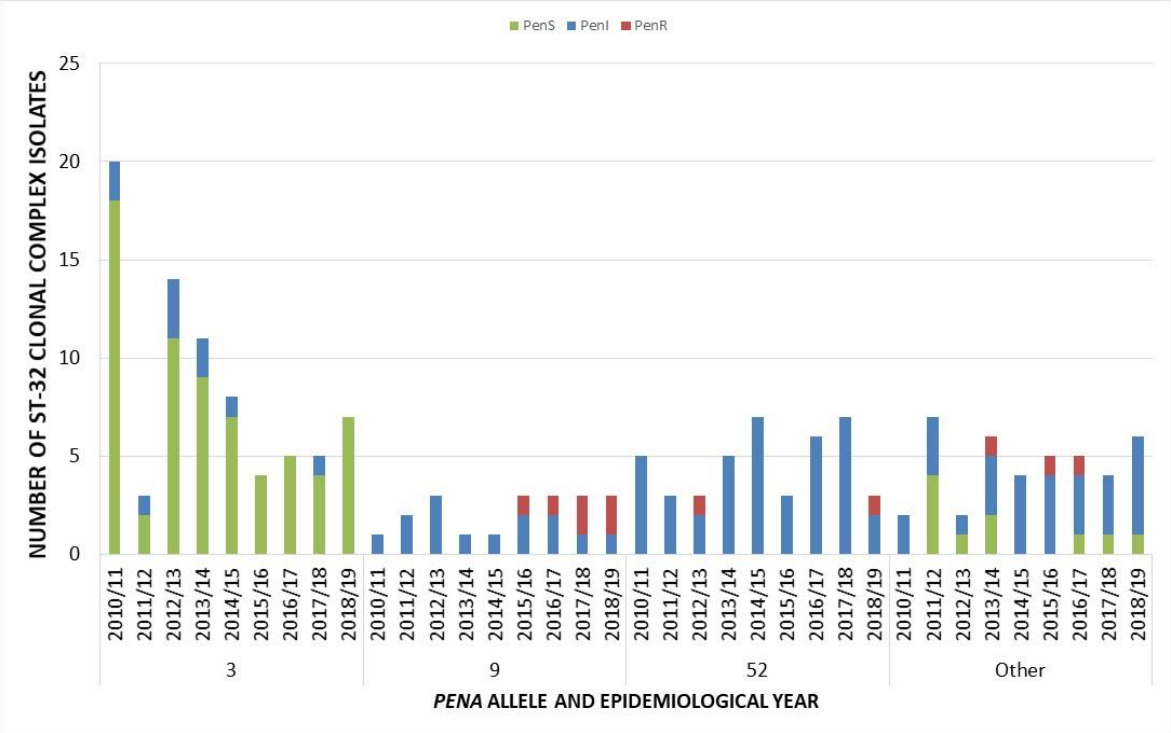
Over the last four years (2015/16-2018/19), an increase was observed in the annual proportion of PenR isolates among ST-32 CC (Figure 3-19), with the highest proportion of PenR isolates in 2018/19 (16%). The annual proportion of PenI isolates has remained relatively stable. The number and proportion of PenS isolates decreased over time. Most ST-32 CC isolates were serogroup B (n=180; 98%). The most prevalent *penA* alleles among serogroup B ST-32 CC isolates were alleles 3, 9 and 52 (Figure 3-20). The number of PenS isolates with *penA3* decreased over the time. An increase in PenR isolates with *penA9* over the last four years was observed.

Figure 3-19: Annual distribution of penicillin susceptibility among ST-32 clonal complex IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.



n=184 ST-32 CC IMD isolates. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

Figure 3-20: Annual distribution of penicillin susceptibility among serogroup B ST-32 clonal complex IMD isolates with the corresponding most prevalent *penA* alleles in England, Wales and Northern Ireland from 2010/11-2018/19.



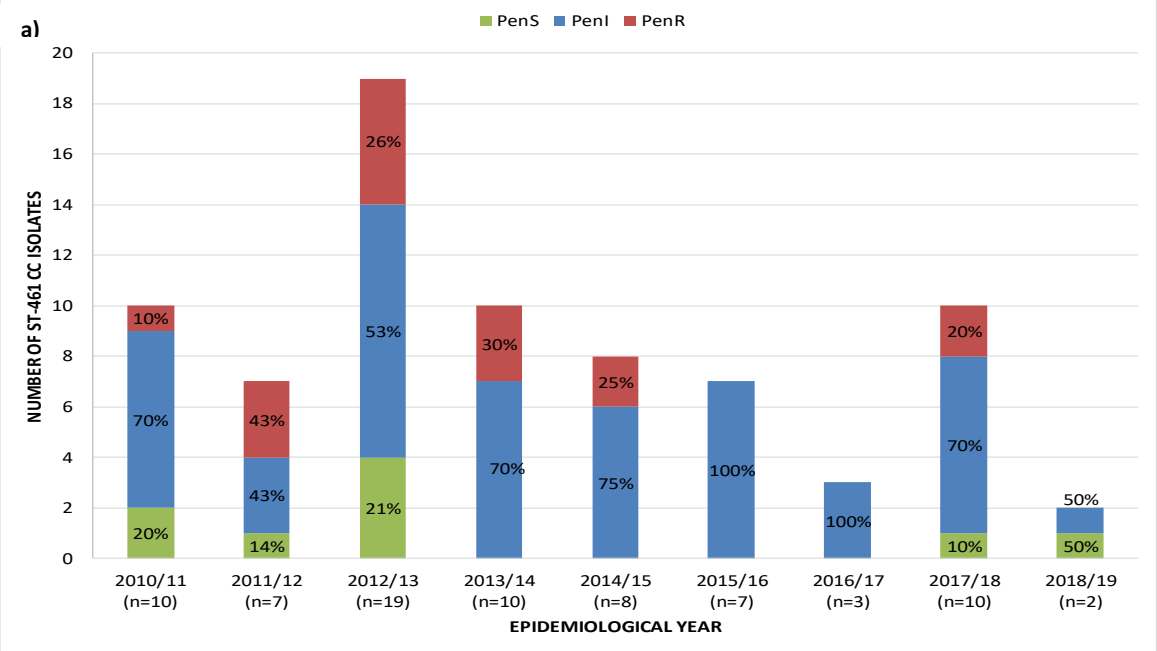
n=180 serogroup B ST-32 clonal complex IMD isolates. PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

3.1.2.4.7 Other main clonal complexes

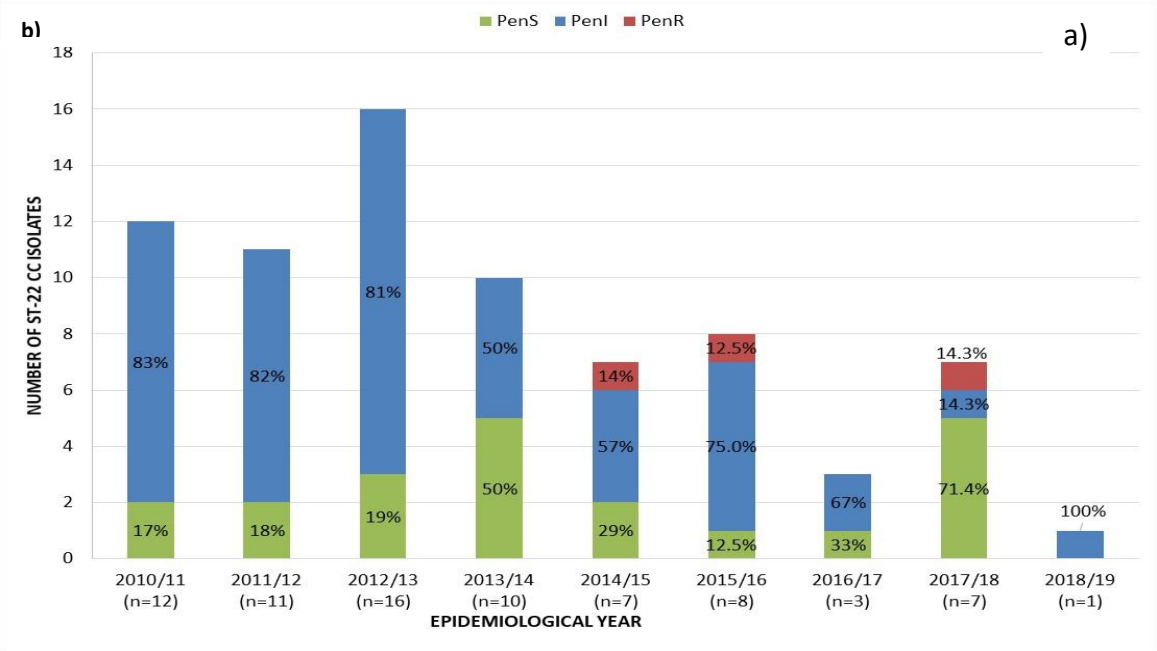
Two percent of IMD isolates received from 2010/11-2018/19 belonged to ST-461 CC and 2% belonged to ST-22 CC. Overall there was a decrease in the number of isolates belonging to these CCs over time (Figure 3-21). PenI isolates represented the greatest proportion of these isolates annually. Thirteen percent of IMD isolates belonged to ST-23 CC and 6% belonged to ST-213 CC. Over the last four years, PenR ST-213 CC IMD isolates have been observed.

Figure 3-21: Annual distribution of penicillin susceptibility among ST-461, ST-22, ST-23 and ST-213 clonal complex IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.

ST-461 clonal complex isolates (n=76)



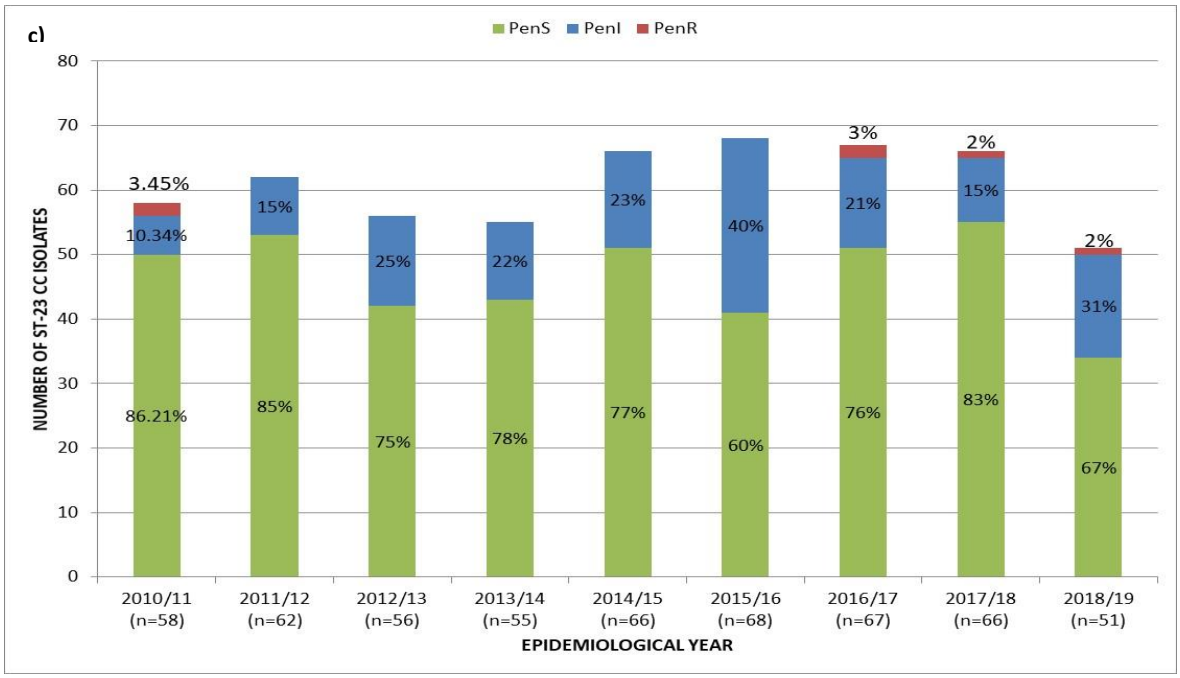
ST-22 clonal complex isolates (n=75)



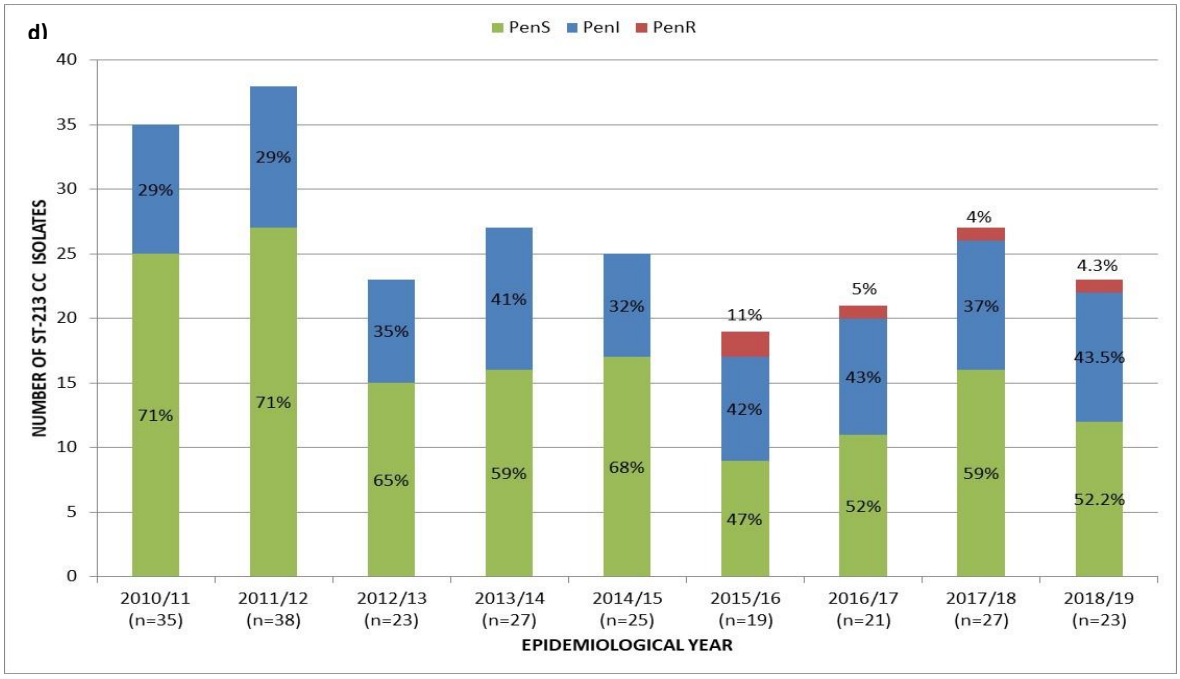
PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

Figure 3-21: (continued).

ST-23 clonal complex isolates (n=549)



ST-213 clonal complex isolates (n=238)



PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines.

3.1.2.5 *PenA171*

One PenR isolate (PubMLST ID 28138; MIC = 0.38 mg/L, beta-lactamase negative) harboured *penA171*. This allele did not contain any of the five AASs associated with conferring reduced susceptibility or resistance to penicillin (F504L, A510V, I515V, H541N, I566V; Appendix 4). It had one AAS when aligned to wild type (WT) allele *penA1;* P551S. Three other *penA* alleles (*penA111*, *penA312 penA324*) with P551S, which also did not contain any of the five AASs associated with conferring reduced susceptibility or resistance to penicillin, were identified on PubMLST (accessed 05/10/2020; Appendix 6). Meningococcal isolates identified on PubMLST with alleles containing P551S alone were not penicillin-resistant (MICs = 0.016–0.094 mg/L) (accessed 05/10/2020; Appendix 7).

The PenR isolate (28138) was serogroup W belonging to ST-11 CC. A genome comparison of this and two closely related PenS isolates (28132 and 28135; Appendix 8) identified a different *mtrR* gene (NEIS1635). The *mtrR* allele harboured by the PenR isolate, *mtrR217,* was not found among any other isolate on PubMLST (accessed 27/10/2020). When aligned to WT *mtrR* allele 1 (Appendix 9), there was one AAS; S32W. Other *mtrR* alleles with this AAS (alleles 190 and 426) and isolates containing these alleles on PubMLST were identified (Table 3-3; accessed 27/10/2020). No other meningococcal isolates with either of these alleles were identified. Gonococcal isolates with *mtrR* alleles 190 (n=16) and 426 (n=3) were identified and, where known, had penicillin MICs of 0.25-4 mg/L. All the gonococcal isolates had *penA85*, which only had three out of the five AASs associated with conferring reduced susceptibility or resistance to penicillin (F504L, A510V, I515V).

Table 3-3: PubMLST isolates harbouring *mtrR* alleles with the amino acid substitution S32W.

ID	Country	Year	Species	Penicillin MIC (mg/L)	*mtrR* allele (NEIS1635)	*penA* allele
28138	UK [England]	2013	Neisseria meningitidis	0.38	217	171
27271	USA	2009	Neisseria gonorrhoeae	4	190	85
37101	USA	2012	Neisseria gonorrhoeae	1	190	85
37125	USA	2007	Neisseria gonorrhoeae	1	190	85
37199	USA	2012	Neisseria gonorrhoeae	1	190	85
37318	USA	2005	Neisseria gonorrhoeae	1	190	85
37341	USA	2006	Neisseria gonorrhoeae	1	190	85
37100	USA	2012	Neisseria gonorrhoeae	0.5	190	85
37104	USA	2012	Neisseria gonorrhoeae	0.5	190	85
37121	USA	2006	Neisseria gonorrhoeae	0.5	190	85
37368	USA	2007	Neisseria gonorrhoeae	0.5	190	85
37103	USA	2012	Neisseria gonorrhoeae	0.25	190	85
36269	Kenya	2012	Neisseria gonorrhoeae	NK	426	664
36273	Kenya	2012	Neisseria gonorrhoeae	NK	426	664
39135	Kenya	2012	Neisseria gonorrhoeae	NK	426	664
48193	UK [England]	2014	Neisseria gonorrhoeae	NK	190	664
48269	UK [England]	2014	Neisseria gonorrhoeae	NK	190	664
48283	UK [England]	2014	Neisseria gonorrhoeae	NK	190	664
74477	Spain	NK	Neisseria gonorrhoeae	NK	190	85
87312	France	2013	Neisseria gonorrhoeae	NK	190	85

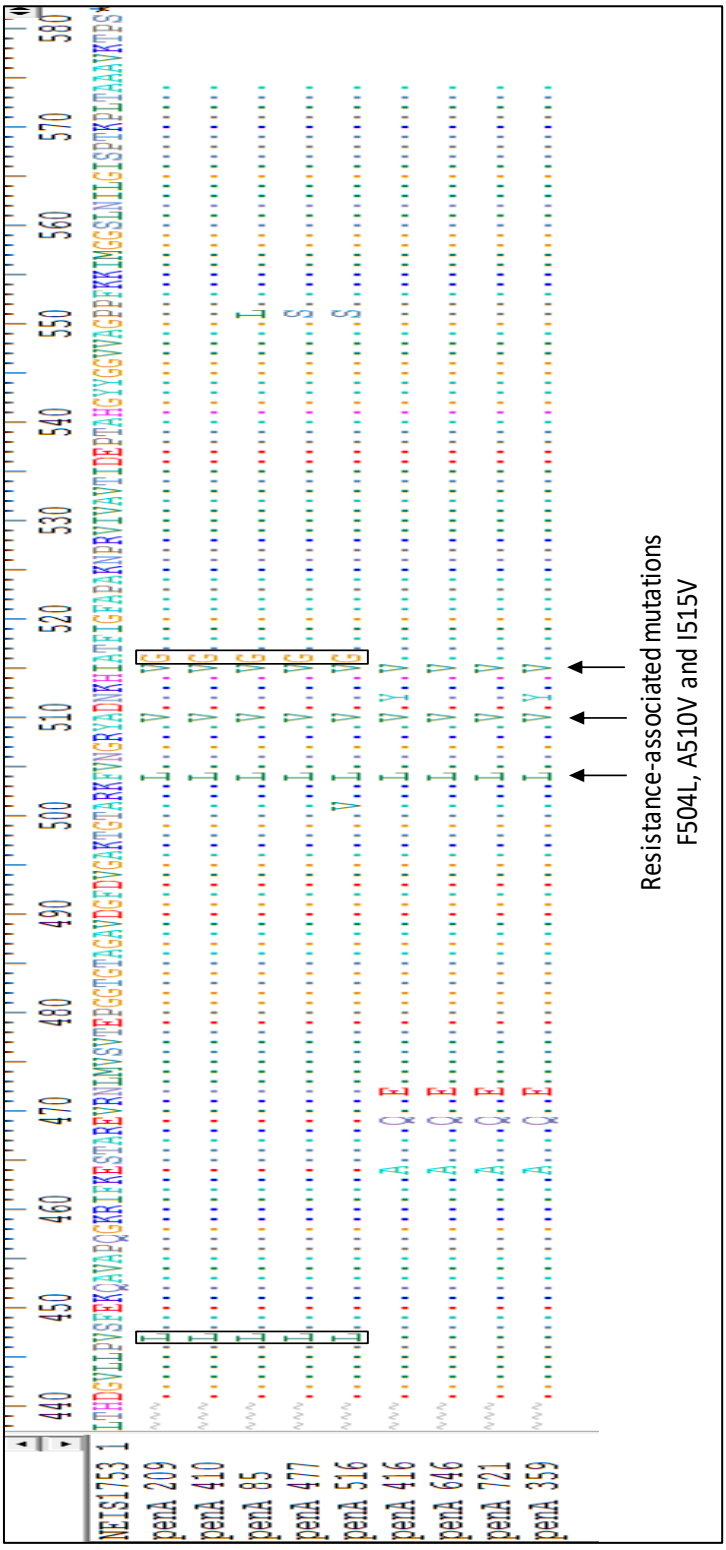
NK = not known.

3.1.2.6 *PenA209*

One PenR isolate (39380; MIC = 0.5 mg/L) harboured *penA209*. This allele had only three out of the five AASs associated with conferring reduced susceptibility or resistance to penicillin (F504L, A510V and I515V; Appendix 4). When aligned to the WT allele *penA1,* the allele had additional AASs at position 447 (V447L) and position 516 (A516G). Other *penA* alleles on PubMLST with the same three out of five AASs (F504L, A510V and I515V) were identified (n=8; Figure 3-22; accessed 30/09/2020; alleles 85, 359, 410, 416, 477, 516, 646 and 721). *PenA* alleles 85, 410, 477 and 516 also harboured A447L and A516G whilst alleles 359, 416, 646 and 721 did not.

Meningococcal isolates harbouring these *penA* alleles were identified on the PubMLST database (n=28; accessed 30/09/2020) (Table 3-4). Penicillin MIC values among these isolates (where available) ranged from 0.047-0.5 mg/L. The MICs of isolates harbouring *penA* alleles with V447L and A516G (n=24) ranged from 0.12–0.5 mg/L whilst those without (n=4) ranged from 0.047-0.094 mg/L. *PenA* alleles containing A447L and A516G were found among gonococcal isolates on PubMLST (*penA85*; n=503, *penA209*; n=878, *penA410*; n=1,832, *penA477*; n=448, *penA516*; n=195; accessed 30/09/2020).

Figure 3-22: Allignment of *penA* alleles harbouring three out of the five amino acid substitutiosns (F504L, A510V, I515V) assocated with conferring reduced susceptilbity or resistance to penicillin.



Wild type allele=NEIS1753_1. Amino acid substitutions V447L and A516G are also indicated (boxed).

Table 3-4: PubMLST meningococcal isolates harbouring *penA* alleles with only three out of the five amino acid substitutions (F504L, A510V and I515V) associated with conferring reduced susceptibility or resistance to penicillin.

ID	Country	Year	Disease	Source	Penicillin MIC (mg/L)	*penA* allele	V447L & A516G
39380	UK [England]	2015	Invasive (unspecified/other)	Blood	0.5	209	Yes
72293	UK [England]	2019	Carrier	Rectal	0.38	209	Yes
72294	UK [England]	2019	Carrier	Rectal	0.38	410	Yes
16983	France	2006	Invasive (unspecified/other)	CSF	0.25	85	Yes
39371	UK [England]	2015	Invasive (unspecified/other)	Blood	0.25	410	Yes
72314	UK [England]	2019	Carrier	Rectal	0.25	209	Yes
20445	UK [England]	2011	Invasive (unspecified/other)	CSF	0.19	410	Yes
35358	UK [Scotland]	2012	Invasive (unspecified/other)	Blood	0.12	209	Yes
31181	UK [England]	2011	Carrier	Rectal	NK	209	Yes
31185	UK [England]	2011	Carrier	Rectal	NK	410	Yes
38957	Italy	2013	Carrier	Throat	NK	209	Yes
59108	USA	2006	Carrier	Throat	NK	209	Yes
59163	USA	2006	Carrier	Throat	NK	209	Yes
59193	USA	2006	Carrier	Throat	NK	209	Yes
59199	USA	2006	Carrier	Throat	NK	209	Yes
59254	USA	2007	Carrier	Throat	NK	209	Yes
59265	USA	2007	Carrier	Throat	NK	209	Yes
61162	Italy	2016	NK	NK	NK	209	Yes
61176	Italy	2016	NK	NK	NK	209	Yes
83723	Sweden	NK	NK	NK	NK	209	Yes
85839	USA	2006	Carrier	Throat	NK	209	Yes
92821	Portugal	2018	Carrier	Throat	NK	209	Yes
94512	Sweden	NK	NK	NK	NK	209	Yes
95841	Sweden	NK	Invasive (unspecified/other)	NK	NK	410	Yes
21104	UK [Wales]	2011	Invasive (unspecified/other)	Blood	0.094	416	No
35474	UK [England]	2013	Invasive (unspecified/other)	Blood	0.094	646	No
44735	UK [England]	2016	Invasive (unspecified/other)	Blood	0.094	721	No
38077	UK [England]	2015	Carrier	Throat	0.064	646	No
18624	France	2011	Invasive (unspecified/other)	CSF	0.047	359	No

CSF = cerebral spinal fluid. NK = not known.

3.1.2.7 *PenA327*

PenA allele 327 was found among one PenR isolate (MIC = 0.38 mg/L), three PenI isolates (MICs = 0.125-0.25 mg/L) and one PenS isolate (MIC = 0.47 mg/L). When aligned to WT allele *penA1*, *penA327* harboured four out of the five AASs associated with conferring reduced susceptibility or resistance to penicillin (F504L, A510V, I515V, H541N). Other *penA* alleles with the same four out of five AASs (n=16) were identified on PubMLST (accessed 24/09/2020, Appendix 10). Meningococcal isolates harbouring any of these *penA* alleles were identified on PubMLST (n=34; Appendix 11). MIC values were known for 12 isolates which were PenS (n=2; alleles 65 and 292; accessed 24/09/2020), PenI (n=8; alleles 178, 330, 372, 387 and 565) and PenR (n=2; alleles 65 and 361). *PenA327* did not share any unique AASs with *penA* alleles among PenR isolates.

PenA327 had an AAS (G545S) that was not present among any other *penA* alleles that had only four out of the five AASs associated with conferring reduced susceptibility or resistance to penicillin. Other *penA* alleles with G545S were identified on PubMLST (n=41; Appendix 12) and all contained all five AASs associated with conferring reduced susceptibility or resistance to penicillin (n=38) or none (n=3). No MIC data were available for isolates on PubMLST harbouring alleles with G545S only.

All five IMD isolates with *penA327* also displayed reduced susceptibility to cefotaxime (0.047 – 0.125 mg/L) (section 3.1.3).

3.1.3 Cefotaxime susceptibility

3.1.3.1 MIC distribution

Of the 4,122 IMD isolates received at the MRU from culture-confirmed cases from July 2010-June 2019, 4,121 were cefotaxime-susceptible (MICs = <0.002–0.125 mg/L and one was cefotaxime-resistant (MIC = 0.25 mg/L; Table 3-5).

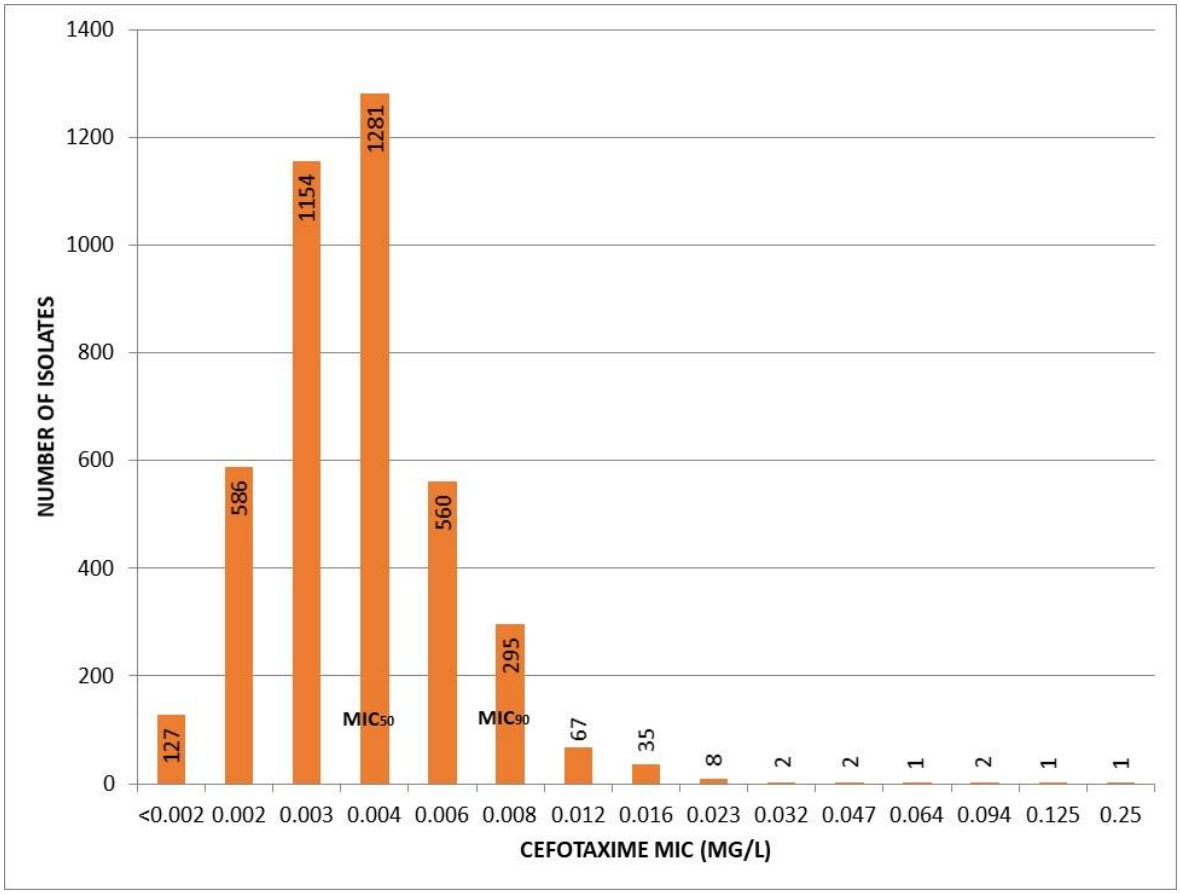
Cefotaxime MIC values of all isolates ranged from <0.002–0.25 mg/L (Figure 3-23). Isolates with MICs of 0.004 mg/L were most common (31%). The MIC_{50} was 0.004 mg/L and the MIC_{90} was 0.008 mg/L.

Table 3-5: Distribution of cefotaxime susceptibility among IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.

	Number of isolates									
	2010/11 (n=500)	**2011/12 (n=400)**	**2012/13 (n=450)**	**2013/14 (n=403)**	**2014/15 (n=505)**	**2015/16 (n=521)**	**2016/17 (n=501)**	**2017/18 (n=488)**	**2018/19 (n=354)**	**Total (n=4,122)**
Cefotaxime-susceptible **≤0.125 mg/L**	499	400	450	403	505	521	501	488	354	4,121
Cefotaxime-resistant **>0.125 mg/L**	1	0	0	0	0	0	0	0	0	1

Cefotaxime susceptibility according to EUCAST guidelines.

Figure 3-23: Cefotaxime MICs among IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.



Out of the 4,122 IMD isolates, only seven had cefotaxime MICs ≥ 0.047 mg/L (0.2%). These isolates harboured *penA327* (n=5), *penA11* (n=1) and *penA419* (n=1). Bar one, isolates were also PenR (0.38-0.5 mg/L) or PenI (0.125-0.25 mg/L). The characteristics of these isolates are displayed in Table 3-6.

Table 3-6: IMD isolates with cefotaxime MICs ≥ 0.047 mg/L in England, Wales and Northern Ireland from 2010/11-2018/19.

PubMLST ID	Serogroup	Clonal complex	Cefotaxime MIC (mg/L)	Penicillin MIC (mg/L)	*penA* allele
35758	B	ST-41/44	0.047	0.047	327
44811	B	INCOMPLETE MLST[a]	0.047	0.5	11
39403	C	ST-11	0.064	0.125	327
41472	C	ST-11	0.094	0.38	327
42499	C	ST-11	0.094	0.19	327
60650	C	ST-11	0.125	0.25	327
20267	B	ST-162	0.25	0.5	419

[a] Exact match for ST-1867 for five loci.

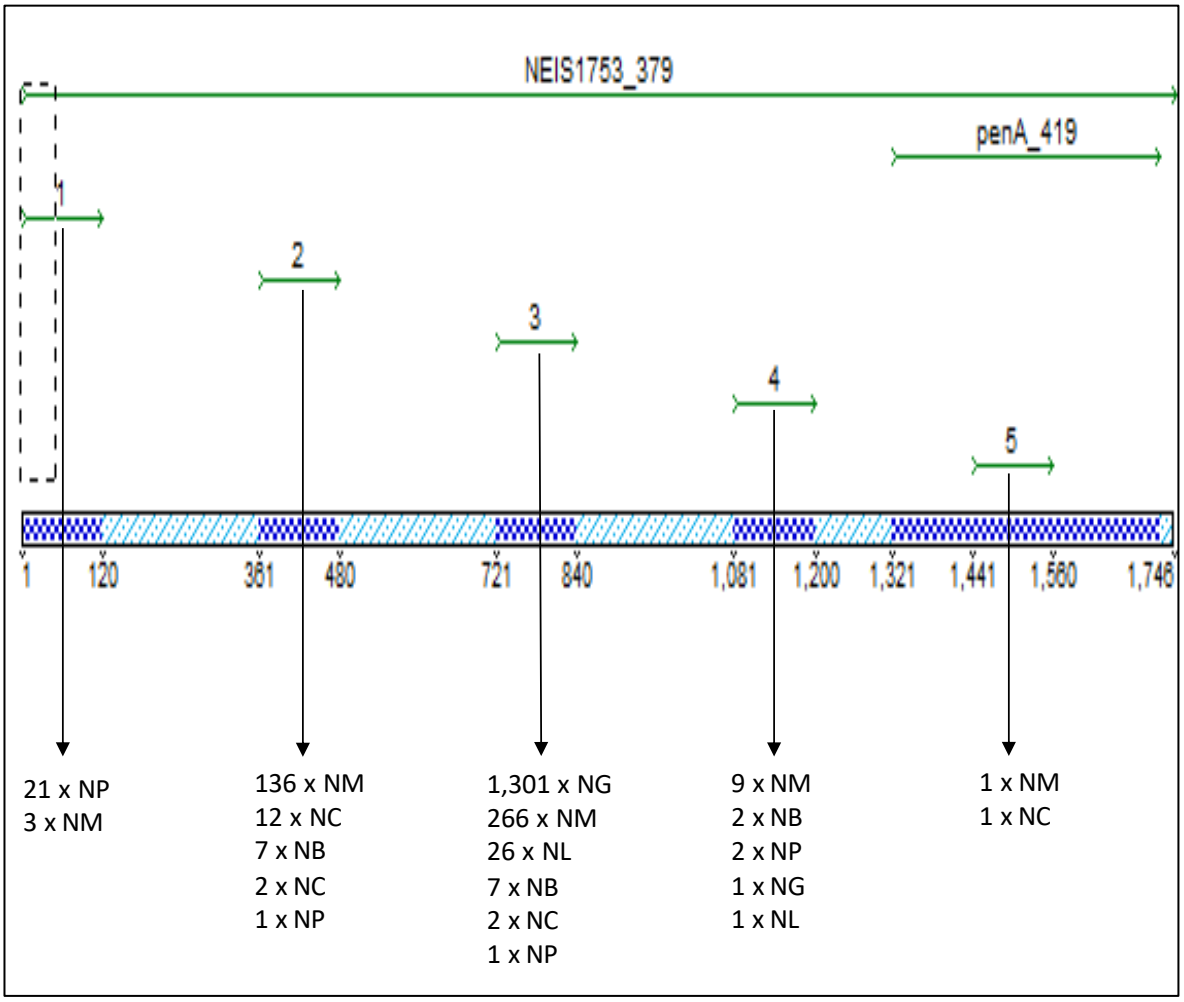
3.1.3.2 Cefotaxime-resistant isolate

One IMD isolate was cefotaxime-resistant (20267; MIC = 0.25 mg/L). It was also penicillin-resistant (MIC = 0.5 mg/L). The isolate belonged to ST-162 CC. A core genome comparison of all ST-162 CC isolates on PubMLST (n=72; 07/10/2020) identified the closest related cefotaxime-susceptible isolates (n=19; Appendix 13). Variable loci between these 20 ST-162 CC isolates and probable recombination sites were determined (Appendix 14). A probable recombination region of 12 loci, corresponding to the cell wall-associated genes, which included the *penA* gene (NEIS1753), was identified. The corresponding alleles were also found among non-pathogenic *Neisseria* isolates on PubMLST (*N. bergeri* and *N. polysaccharea*).

3.1.3.2.1 *penA* allele in cefotaxime isolate 20267

The *penA* gene harboured by the cefotaxime-resistant isolate (NEIS1753 allele 379; *penA419*) was not found in any other isolate on PubMLST. Five equidistant fragments (120 bp each) from across the length of NEIS1753 allele 379 shared 100% identity with those of several other commensal species (Fragments 1-5; Figure 3-24).

Figure 3-24: Five fragments of NEIS1753 allele 379 and species with sequences with 100% identity to that of the fragments.

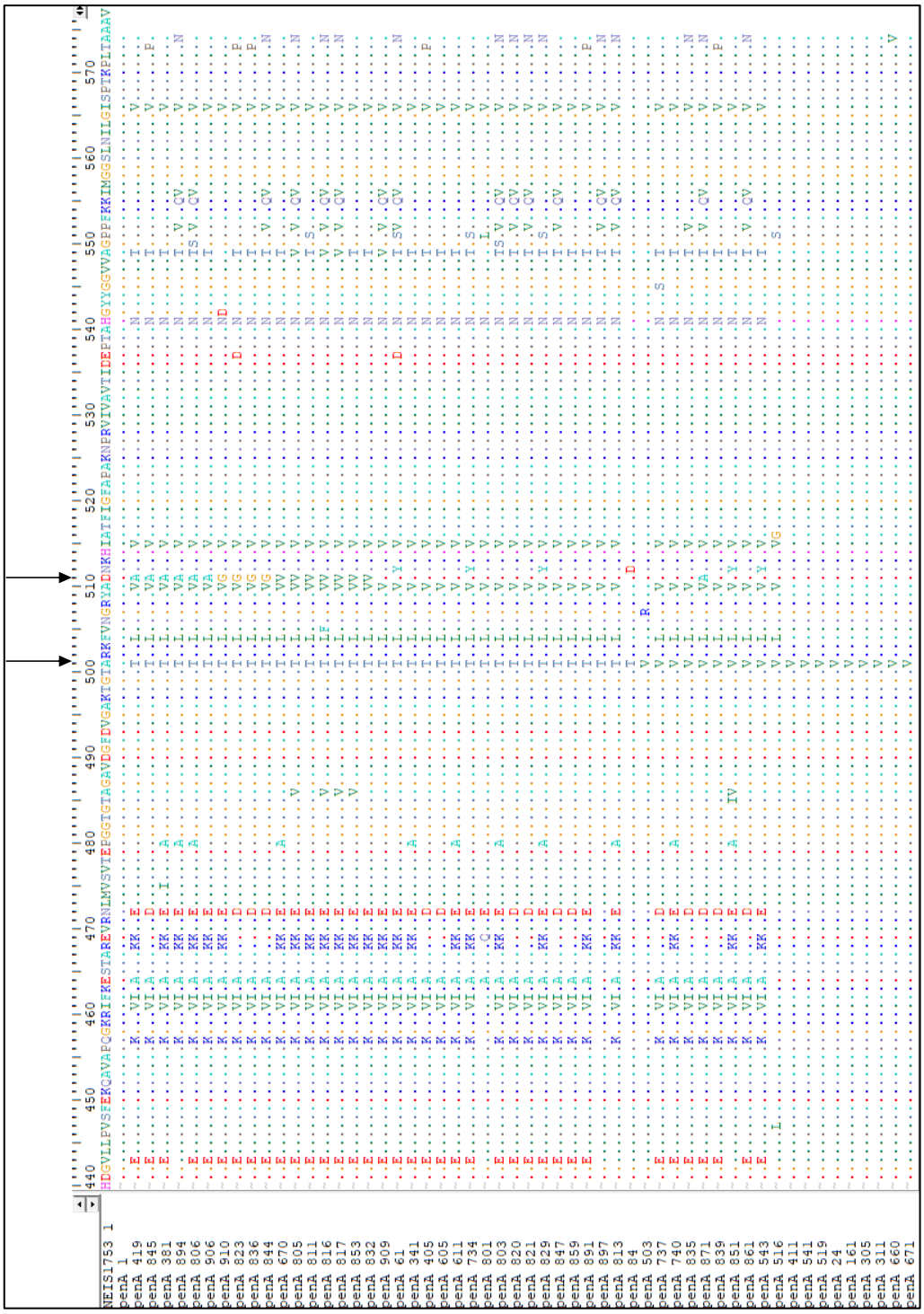


Isolates identified on PubMLST. 1 = bp 1-120 of NEIS1753 allele 379, 2 = bp 361-480, 3 = bp 721-840, 4 = bp 1201-1320 5 = bp 1441-1560 of NEIS1753_379. NB = *N. bergeri*, NC = *N. cinerea*, NG = *N. gonorrhoea*, NM = *N. meningitidis*, NL= *N. lactamica*, NP = *N. polysaccharea*. The scale bar indicates the bp position.

When aligned to WT NEIS1753 allele 1, NEIS1753 allele 379 had two unique AAS that were not found among those alleles harboured by cefotaxime-susceptible PenR isolates (and therefore containing the five AASs associated with conferring reduced susceptibility or resistance to penicillin) (Appendix 15). The two unique AASs were A501T and D511A. Both AASs fell within the 402 bp fragment of NEIS1753_379; *penA419*. Other *penA* alleles harbouring either of these mutations (n=56; Figure 3-25) and isolates harbouring these

alleles on PubMLST were identified (n=69; Table 3-7). Among these were *N. meningitidis* (n=50), *N. lactamica* (n=5) and *N. polysaccharea* (n=1) isolates. All *penA* alleles harboured by these isolates had the AAS at position 501; A501T (n=17) or A501V (n=39). Six isolates harbouring a *penA* allele with A501T had an additional AAS at position 511; D511A (*penA419*; n=1), D511G (*penA910*; n=2, *penA836*; n=1) or D511V (*penA670*; n=1, *penA805*; n=1). Where known, cefotaxime MICs of isolates with A501V mutation were 0.003-0.012 mg/L. Isolates with the A501T mutation had MICs of 0.016-0.125 mg/L. Isolates with both A501T and D511 mutations had MICs of 0.125-0.5 mg/L.

Figure 3-25: Alignment of *penA419* with a wild type *penA* allele and *penA* alleles harbouring amino acid substitutions at position A501 and/or D511.



PenA alleles identified on PubMLST. Amino acid positions 501 and 511 are highlighted. The scale bar indicates the amino acid position.

Table 3-7: PubMLST isolates harbouring *penA* alleles with amino acid substitutions at amino acid position 501 and/or 511.

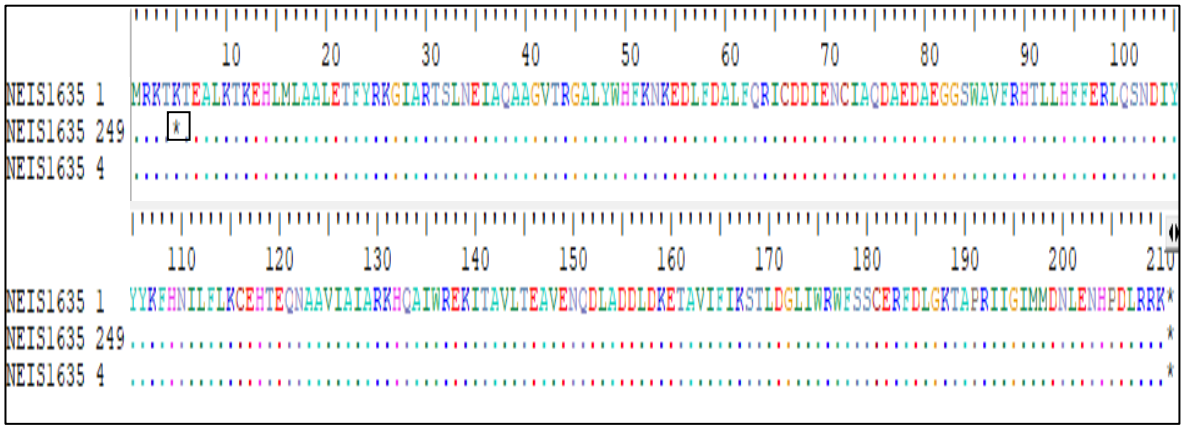
Year	Disease	Site	Species	Penicillin MIC (mg/L)	Cefotaxime MIC (mg/L)	*penA* allele	A501 mutation	D511 mutation	Other 5 AASs associated with PenR and PenI isolates
2011	Invasive (unspecified/other)	Blood	Neisseria menigitidis	0.5	0.25	419	A501T	D511A	Yes
2020	Meningitis and septicaemia	NK	Neisseria menigitidis	0.5	0.125	910	A501T	D511G	Yes
2020	Meningitis and septicaemia	NK	Neisseria menigitidis	0.5	0.19	910	A501T	D511G	Yes
2015	Carrier	Throat swab	Neisseria lactamica	NK	NK	836	A501T	D511G	Yes
2013	Carrier	Throat swab	Neisseria menigitidis	NK	NK	670	A501T	D511V	Yes
2015	NK	NK	Neisseria polysaccharea	NK	NK	805	A501T	D511V	Yes
2016	Meningitis	Blood	Neisseria menigitidis	0.25	0.047	909	A501T	None	Yes
2016	Meningitis	Blood	Neisseria menigitidis	0.5	0.047	909	A501T	None	Yes
1961	Invasive (unspecified/other)	CSF	Neisseria menigitidis	0.016	NK	84	A501T	None	No
2010	Invasive (unspecified/other)	CSF	Neisseria menigitidis	0.125	0.047	341	A501T	None	Yes
2005	Invasive (unspecified/other)	CSF	Neisseria menigitidis	0.38	0.125	61	A501T	None	Yes
2016	Invasive (unspecified/other)	NK	Neisseria menigitidis	0.38	0.016	734	A501T	None	Yes
2013	Invasive (unspecified/other)	Blood	Neisseria menigitidis	0.012	0.004	24	A501V	None	No
2011	Invasive (unspecified/other)	CSF	Neisseria menigitidis	0.015	0.004	24	A501V	None	No
2010	Invasive (unspecified/other)	Blood	Neisseria menigitidis	0.023	0.004	411	A501V	None	No
2013	Invasive (unspecified/other)	Blood	Neisseria menigitidis	0.023	0.008	311	A501V	None	No
2011	Septicaemia	Blood	Neisseria menigitidis	0.023	0.06	311	A501V	None	No
2011	Invasive (unspecified/other)	Blood	Neisseria menigitidis	0.032	0.003	311	A501V	None	No
2017	Invasive (unspecified/other)	Blood	Neisseria menigitidis	0.032	0.006	161	A501V	None	No
2011	Septicaemia	Blood	Neisseria menigitidis	0.032	0.008	311	A501V	None	No
2015	Invasive (unspecified/other)	Blood	Neisseria menigitidis	0.032	0.008	311	A501V	None	No
2017	Invasive (unspecified/other)	Blood	Neisseria menigitidis	0.032	0.008	161	A501V	None	No
NK	Invasive (unspecified/other)	Blood	Neisseria menigitidis	0.047	0.006	24	A501V	None	No
2016	Invasive (unspecified/other)	Blood	Neisseria menigitidis	0.047	0.006	671	A501V	None	No
2014	Invasive (unspecified/other)	Blood	Neisseria menigitidis	0.047	0.012	24	A501V	None	No
2011	Invasive (unspecified/other)	Blood	Neisseria menigitidis	0.064	0.008	24	A501V	None	No
2004	Invasive (unspecified/other)	CSF	Neisseria menigitidis	0.094	NK	24	A501V	None	No
2016	Meningitis	CSF	Neisseria menigitidis	NK	NK	61	A501T	None	Yes
2014	Carrier	Throat swab	Neisseria lactamica	NK	NK	605	A501T	None	Yes
2015	Carrier	Throat swab	Neisseria lactamica	NK	NK	611	A501T	None	Yes
2015	Carrier	Throat swab	Neisseria lactamica	NK	NK	611	A501T	None	Yes
2015	Carrier	Throat swab	Neisseria lactamica	NK	NK	611	A501T	None	Yes
1999	Carrier	Throat swab	Neisseria menigitidis	NK	NK	311	A501V	None	No
2001	Invasive (unspecified/other)	CSF	Neisseria menigitidis	NK	NK	161	A501V	None	No
2010	Invasive (unspecified/other)	Blood	Neisseria menigitidis	NK	NK	311	A501V	None	No
NK	NK	Throat swab	Neisseria menigitidis	NK	NK	503	A501V	None	No
1998	NK	NK	Neisseria menigitidis	NK	NK	24	A501V	None	No
2013	Invasive (unspecified/other)	Blood	Neisseria menigitidis	NK	NK	411	A501V	None	No
2006	Invasive (unspecified/other)	NK	Neisseria menigitidis	NK	NK	519	A501V	None	No
2005	Invasive (unspecified/other)	NK	Neisseria menigitidis	NK	NK	311	A501V	None	No
2014	Invasive (unspecified/other)	Blood	Neisseria menigitidis	NK	NK	311	A501V	None	No
2013	Invasive (unspecified/other)	Blood	Neisseria menigitidis	NK	NK	161	A501V	None	No
2015	NK	NK	Neisseria menigitidis	NK	NK	660	A501V	None	No
2013	NK	NK	Neisseria menigitidis	NK	NK	311	A501V	None	No
2013	NK	NK	Neisseria menigitidis	NK	NK	311	A501V	None	No
2016	Invasive (unspecified/other)	Blood	Neisseria menigitidis	NK	NK	24	A501V	None	No
2015	Carrier	Throat swab	Neisseria menigitidis	NK	NK	740	A501V	None	Yes
NK	NK	NK	Neisseria menigitidis	NK	NK	311	A501V	None	No
2015	Carrier	Throat swab	Neisseria menigitidis	NK	NK	740	A501V	None	No
2015	Carrier	Throat swab	Neisseria menigitidis	NK	NK	740	A501V	None	No
2017	NK	NK	Neisseria menigitidis	NK	NK	311	A501V	None	No
2012	Meningitis	Blood	Neisseria menigitidis	NK	NK	311	A501V	None	No
2004	NK	NK	Neisseria menigitidis	NK	NK	24	A501V	None	No
1999	Carrier	throat swab	Neisseria menigitidis	NK	NK	671	A501V	None	No
NK	NK	NK	Neisseria menigitidis	NK	NK	311	A501V	None	No
2007	Invasive (unspecified/other)	Sputum	Neisseria menigitidis	NK	NK	311	A501V	None	No
1960	NK	NK	Neisseria animalis	NK	NK	502	None	A511S	No
NK	NK	NK	Neisseria wadsworthii	NK	NK	504	None	A511N	No
2014	NK	NK	Neisseria musculi	NK	NK	524	None	A511S	No
2014	NK	NK	Neisseria musculi	NK	NK	524	None	A511S	No
2014	NK	NK	Neisseria musculi	NK	NK	524	None	A511S	No
2014	NK	NK	Neisseria musculi	NK	NK	524	None	A511S	No
2014	NK	NK	Neisseria musculi	NK	NK	524	None	A511S	No
2014	NK	NK	Neisseria musculi	NK	NK	524	None	A511S	No
2014	NK	NK	Neisseria musculi	NK	NK	524	None	A511S	No
2014	NK	NK	Neisseria musculi	NK	NK	524	None	A511S	No
1999	NK	NK	Neisseria canis	NK	NK	521	None	A511N	No
1962	NK	NK	Neisseria canis	NK	NK	521	None	A511N	No
1974	NK	NK	Neisseria weaveri	NK	NK	501	None	A511S	No

NK = not known. AASs = amino acid substitutions.

3.1.3.2.2 *MtrR* allele in cefotaxime-resistant isolates 20267

The *mtrR* gene (NIES1635) was one of the variable loci identified between the cefotaxime-resistant isolate and the closely related cefotaxime-susceptible isolates. The cefotaxime-resistant isolate harboured *mtrR249* whilst all susceptible isolates harboured *mtrR4.* No other isolate on PubMLST had *mtrR249*. When aligned to a WT *mtrR* allele, *mtrR4* had the same AA sequence, whereas *mtrR249* had a frameshift at AA position five (Figure 3-26). Other *mtrR* alleles with a frameshift at the beginning of the gene (first 60 AAs) were identified (n=13; Appendix 16). Frameshifts among these alleles were at AA positions later than position five. Isolates harbouring these *mtrR* alleles on PubMLST (n=17; alleles 244, 246, 248, 252, 259 or 266) were cefotaxime-susceptible (MICs = <0.002-0.008 mg/L; Appendix 17).

Figure 3-26: *MtrR249* alignment with a wild type *mtrR* allele and *mtrR4*.



NEIS1635 1 = wild type *mtrR* allele. The scale bar indicates the amino acid position. *=frameshift.

3.1.3.3 Elevated cefotaxime MICs

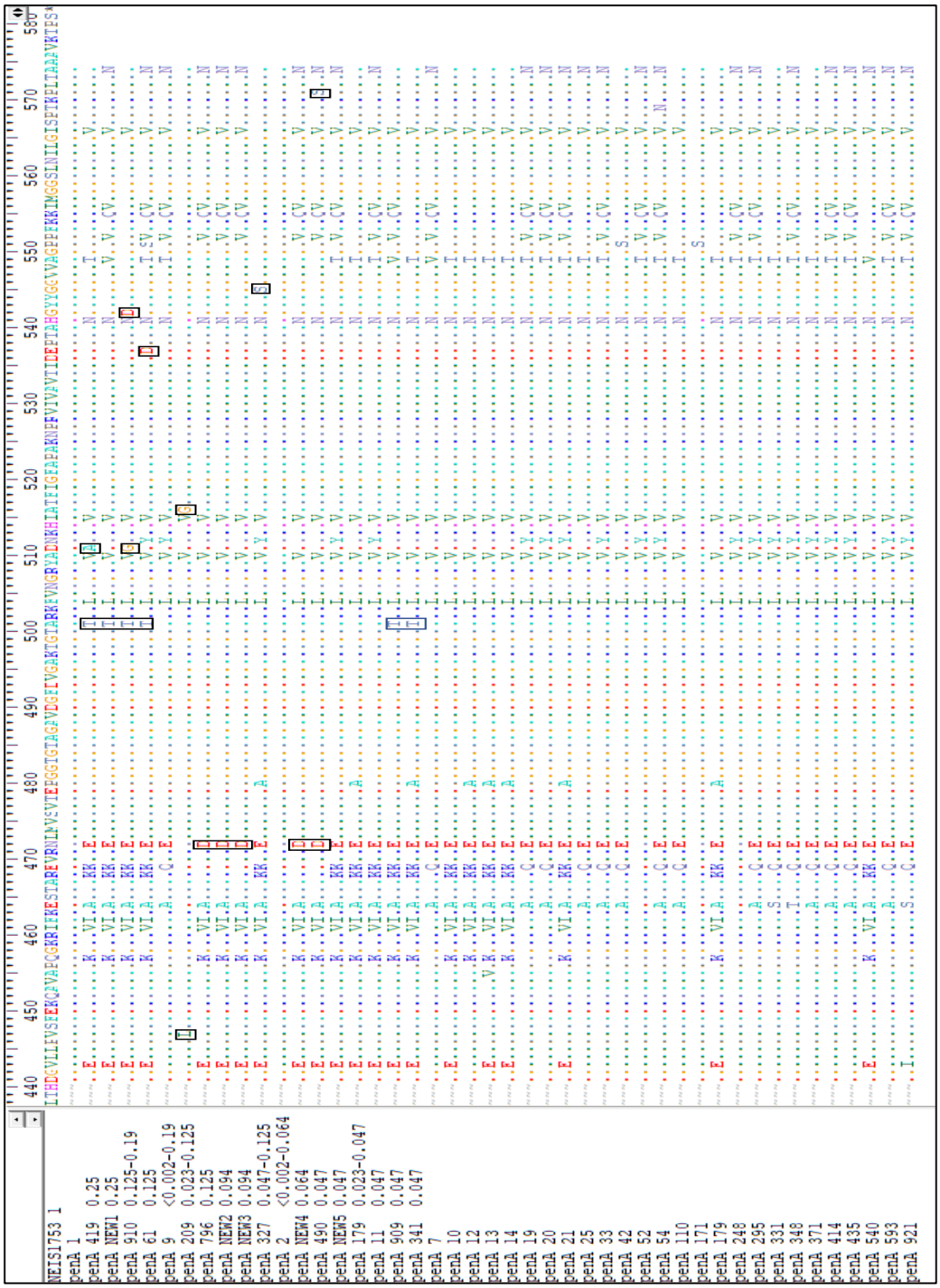
In addition to the isolates previously identified (section 3.1.3) with elevated cefotaxime MICs, 14 non-IMD (non-MGL) isolates with elevated cefotaxime MICs (≥ 0.047 mg/L) were identified at the MRU (Table 3-8) and underwent PCR analysis for *penA* allele determination. All *penA* alleles found among these isolates, along with those alleles previously identified among isolates with known elevated cefotaxime MICs were aligned with a WT *penA* allele (Figure 3-27). *PenA* alleles harboured by cefotaxime-susceptible PenR isolates were also included in the alignment (and therefore contained the five AASs associated with conferring reduced susceptibility or resistance to penicillin). *PenA* AASs unique to those harboured by isolates with cefotaxime MIC values ≥0.047 mg/L compared to those with cefotaxime MICs <0.047 mg/L were identified (Table 3-9; V417L, N472D, A501T, D511A/G, A516G, E537D, G545S, P571S). MICs of isolates harbouring alleles with A501T were 0.047-0.25 mg/L. MICs of isolates harbouring alleles with AASs at D511 in addition to A501T were 0.125-0.25 mg/L. MICs of isolates harbouring alleles with N572D were 0.047-0.125 mg/L.

Table 3-8: Non-IMD (non-MGL) MRU isolates with cefotaxime MICs ≥0.047 mg/L.

Isolate	Organism	Site	Group	Type	Subtype VR1	Subtype VR2	Subtype VR3	Peniclin MIC (mg/L)	Rifampicin MIC (mg/L)	Ciprofloxacin MIC (mg/L)	Cefotaxime MIC (mg/L)	*penA* allele
M17 240186	Neisseria spp	Eye swab						1.5	1.0	0.25	0.25	NEW1
M14 240600	Neisseria meningitidis	Urethral swab	W	2A	NT	P1.2	NT	0.38	0.012	0.006	0.19	9
M15 240173	Neisseria meningitidis	Throat swab	NG	NT	NT	NT	P1.6	0.19	0.023	0.004	0.125	209
M13 240711	Neisseria spp	Eye swab	NG	NT	NT	NT	NT	1.0	0.5	0.023	0.125	796
M11 240095	Neisseria cinerea	Blood						1.5	0.5	0.008	0.094	NEW2
M13 240159	Neisseria spp	Blood						1.5	0.38	0.008	0.094	NEW3
M17 240460	Neisseria meningitidis	Blood	C	2A	P1.5	NT	NT	0.25	0.016	0.008	0.094	327
M13 240621	Neisseria meningitidis	Sputum	Y	NT	P1.5	NT	NT	0.38	0.003	0.006	0.064	2
M16 240658	Neisseria polysaccharae	Blood						1.0	0.38	0.003	0.064	NEW4
M20 240247	Neisseria meningitidis	Blood	C	2A	NT	NT	NT	0.38	0.047	0.002	0.064	327
M14 240642	Neisseria spp	Blood						0.75	1.0	0.023	0.047	490
M15 240571	Neisseria spp	Bronchoaveolar Lavage						1.0	1.0	0.012	0.047	NEW5
M15 240293	Neisseria meningitidis	Throat swab	NG	NT	P1.12	NT	NT	0.5	0.094	0.008	0.047	179
M19 240153	Neisseria meningitidis	Sputum	NG	NT	P1.7	NT	NT	2.0	0.064	0.006	0.047	11

Five *penA* sequences not yet assigned a PubMLST *penA* allele ID are termed NEW1-5. NK= not known. NT = non-typable. NG= non-groupable.

Figure 3-27: *PenA* alleles harbored by isolates with cefotaxime MICs ≥0.047 mg/L and alleles harboured by cefotaxime-susceptible penicillin-resistant isolates.



PenA alleles identified in this study. *PenA* NEW1-5 alleles identified by PCR and sanger sequencing among non-IMD isolates yet to be assigned a PubMLST *penA* allele ID (Table 3-8). Amino acid substitutions unique to alleles with isolates displaying elevated cefotaxime resistance are highlighted (boxed).

Table 3-9: *PenA* alleles identified among *Neisseria* isolates with cefotaxime MICs ≥0.047 mg/L.

penA allele	Cefotaxime MIC value or range (mg/L)	Unique *penA* mutations*	Species distribution on PubMLST^
419	0.25	A501T, D511A	1 x NM
NEW1	0.25	A501T	1 x NS
910	0.125-0.19	A501T, D511G, G541D	2 x NM
61	0.125	A501T, E537D	2 x NM
9	<0.002-0.19	None	779 x NM, 40 x NG, 35 x NL, 4 x NC, 4 x NP, 1 x NB
209	0.023-0.125	V447L, A516G	838 x NG, 18 x NM
796	0.125	N572D	2 x NMu
NEW2	0.094	N572D	1 x NC
NEW3	0.094	N572D	1 x NS
327	0.047-0.125	G545S	958 x NG, 50 x NM
2	<0.002-0.064	None	901 x NM, 1 x NG
NEW4	0.064	N572D	1 x NP
490	0.047	N572D, P571S	2 x NMu
NEW5	0.047	None	1 x NS
179	0.023-0.047	None	16 x NM, 6 x NG
11	0.047	None	39 x NM
909	0.047	A501T	2 x NM
341	0.047	A501T	1 x NM

PenA NEW1-5 alleles identified by PCR and sanger sequencing among non-IMD isolates yet to be assigned a PubMLST *penA* allele ID (Table 3-8). NB = *N. bergeri*, NC = *N. cinerea*, NG = *N. gonorrhoea*, NM = *N. meningitidis*, Nmu = *N. mucosa* NL= *N. lactamica*, NP = *N. polysaccharea*, NS = *N. species.* * = unique mutations of *penA* alleles found among isolates with cefotaxime MICs ≥0.047 mg/L compared to those found among PenR isolates with cefotaxime MICs <0.047 mg/L. ^ New1-5 *penA* alleles among species identified at the MRU.

3.1.4 Rifampicin susceptibility

3.1.4.1 MIC distribution

Of the 4,122 IMD isolates received at the MRU from culture-confirmed cases from July 2010 - June 2019, 4,120 (99.95%) were rifampicin-susceptible (MICs = <0.002-0.25 mg/L) and two (0.05%) were rifampicin-resistant (MICs = 0.5 and >32 mg/L). Rifampicin-resistant isolates were received in epidemiological years 2012/13 (n=1) and 2015/16 (n=1) (Table 3-10).

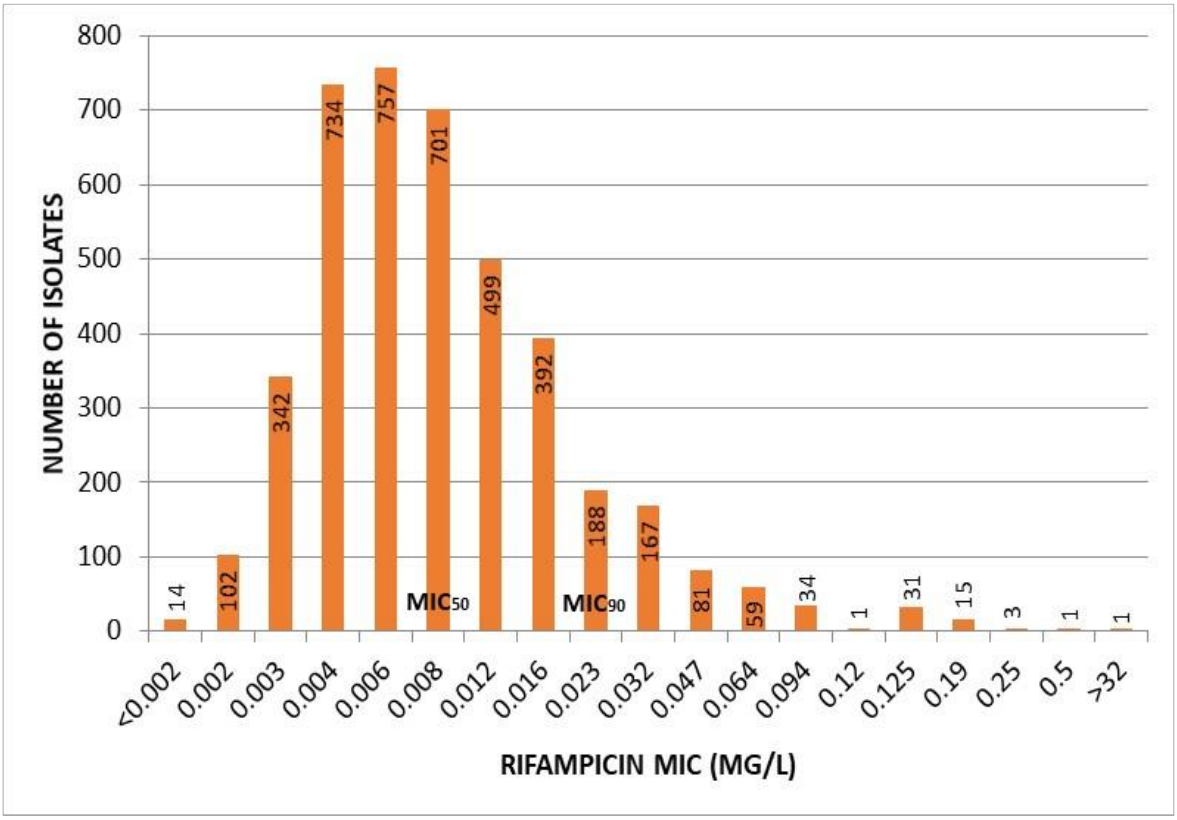
Rifampicin MIC values of all IMD isolates ranged from <0.002 - >32 mg/L (Figure 3-28). Isolates with MICs of 0.006 mg/L were most common, representing 18% of all isolates. The MIC_{50} was 0.008 mg/L and the MIC_{90} was 0.023 mg/L.

Table 3-10: Distribution of rifampicin susceptibility among IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.

	Number of isolates									
	2010/11 (n=500)	**2011/12 (n=400)**	**2012/13 (n=450)**	**2013/14 (n=403)**	**2014/15 (n=505)**	**2015/16 (n=521)**	**2016/17 (n=501)**	**2017/18 (n=488)**	**2018/19 (n=354)**	**Total (n=4,122)**
Rifampicin-susceptible **≤0.25 mg/L**	500	400	449	403	505	520	501	488	354	4,120
Rifampicin-resistant **>0.25 mg/L**	0	0	1	0	0	1	0	0	0	2

Rifampicin susceptibility categorisation according to EUCAST guidelines.

Figure 3-28: Rifampicin MICs among IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.



3.1.4.2 *RpoB* allele distribution

The 659 bp *rpoB* fragment of the NEIS0123 gene, corresponding to AA residues 455-674, was obtained for the 4,122 IMD isolates received at the MRU from 2010/11-2018/19. Fifty-nine *rpoB* alleles were identified among the 4,122 IMD isolates, with frequencies of isolates varying from one to 1,035 (Appendix 18). The most prevalent allele was *rpoB9* (n=1,035; 25%) followed by *rpoB34* (n=834, 20%). Two different *rpoB* alleles were identified among the two rifampicin-resistant isolates: *rpoB84* (MIC = >32 mg/L) and *rpoB238* (MIC = 0.5 mg/L). These alleles were not harboured by any other isolate from E, W and NI, 2010/11-2018/19.

3.1.4.3 Rifampicin-resistant isolates

The characteristics of the rifampicin-resistant isolates are listed in Table 3-11. When aligned to a WT *rpoB* allele (Appendix 19), the resistance-associated alleles (*rpoB84* and *rpoB238*) harboured rifampicin resistance-associated mutations D545E or H555N; referred to as AA positions 542 and 552 in the literature (Stefanelli et al., 2001; Taha et al., 2010).

There was no evidence that suggested either of the two isolates were from close contacts of index cases.

Table 3-11: Characteristics of rifampicin-resistant isolates in England, Wales and Northern Ireland from 2010/11-2018/19.

ID	Epi Year	Serogroup	CC	Rifampicin MIC (mg/L)	*rpoB* allele	*rpoB* mutations	*mtrR* allele
27900	2012/13	B	ST-41/11	>32	84	H555N, I624V, D625N, S654K	9
42499	2015/16	C	ST-11	0.5	238	D545E	21

Epi = Epidemiological. CC = Clonal complex

3.1.5 Ciprofloxacin susceptibility

3.1.5.1 MIC distribution

Of the 4,122 IMD isolates received at the MRU from culture-confirmed cases from July 2010 - June 2019, 4,117 (99.9%) were ciprofloxacin-susceptible (MICs = <0.002-0.03 mg/L) and five (0.1%) were ciprofloxacin-resistant (MICs = 0.06-0.5 mg/L). Ciprofloxacin-resistant isolates were received in epidemiological years 2010/11 (n=1), 2014/15 (n=2), and 2018/19 (n=2) (Table 3-12).

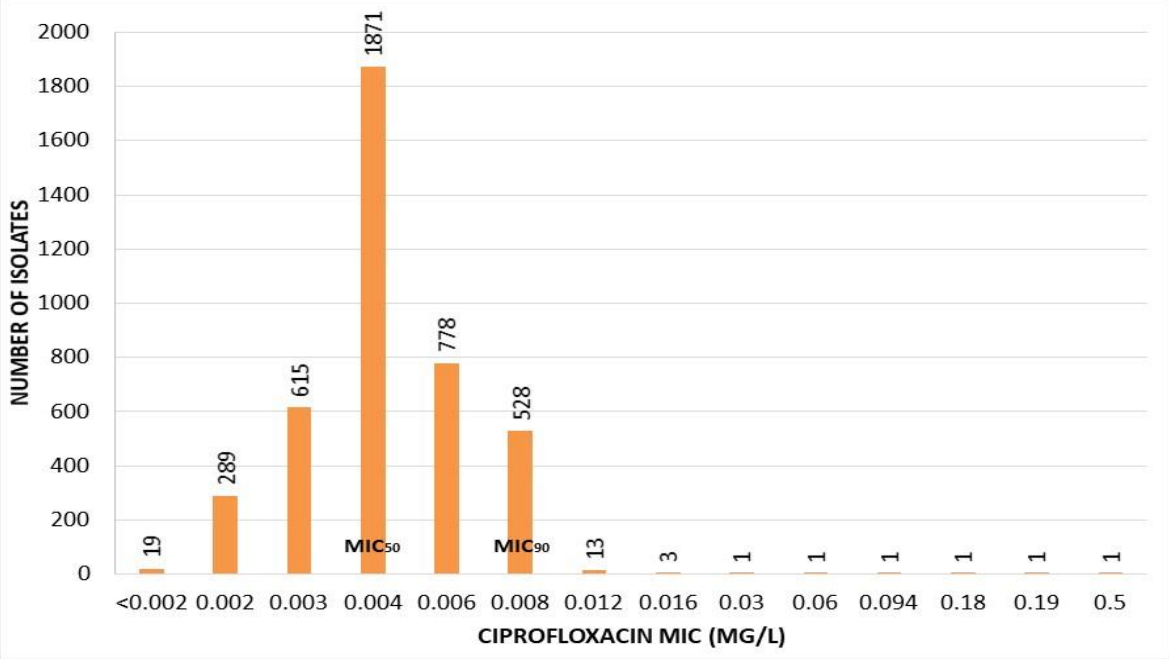
Ciprofloxacin MIC values of all IMD isolates ranged from <0.002 - 0.5 mg/L (Figure 3-29). Isolates with MICs of 0.004 mg/L were most common, representing 45% of all isolates. The MIC_{50} was 0.004 mg/L and the MIC_{90} was 0.008 mg/L.

Table 3-12: Distribution of ciprofloxacin susceptibility among IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.

	Number of isolates									
	2010/11 (n=500)	2011/12 (n=400)	2012/13 (n=450)	2013/14 (n=403)	2014/15 (n=505)	2015/16 (n=521)	2016/17 (n=501)	2017/18 (n=488)	2018/19 (n=354)	Total (n=4,122)
Ciprofloxacin -susceptible ≤0.03 mg/L	499	400	450	403	503	521	501	488	352	4,117
Ciprofloxacin -resistant >0.03 mg/L	1	0	0	0	2	0	0	0	2	5

Ciprofloxacin susceptibility categorisation according to EUCAST guidelines.

Figure 3-29: Ciprofloxacin MICs among IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.



3.1.5.2 *GyrA* allele distribution

The 524 bp *gyrA* fragment of the NEIS1320 gene, corresponding to AA residues 39-213, was obtained for the 4,122 IMD isolates received at the MRU from 2010/11-2018/19. Thirty-six *gyrA* alleles were identified among the 4,122 IMD isolates, with frequencies of isolates varying from 1 to 2,072 (Appendix 20). The *gyrA* alleles of two isolates were not known. The most prevalent allele was *gyrA4* (n=2,072; 50%) followed by *gyrA12* (n=626, 15%). Five different *gyrA* alleles were identified among the five ciprofloxacin resistance isolates; *gyrA6* (MIC = 0.5 mg/L), *gyrA8* (MIC = 0.18 mg/L), *gyrA10* (MIC = 0.094 mg/L), *gyrA146* (MIC = 0.19 mg/L) and *gyrA296* (MIC = 0.06 mg/L). These alleles were not harboured by any other IMD isolate from E, W and NI (2010/11 – 2018/9).

3.1.5.3 Ciprofloxacin-resistant isolates

The ciprofloxacin-resistant isolates all belonged to different clonal complexes (Table 3-13). When aligned to a WT *gyrA* allele (Appendix 21), the resistance-associated alleles (6, 8, 10, 146, 266) harboured one of the ciprofloxacin resistance-associated mutations; either D95N (n=2; MICs = 0.06–0.094 mg/L) or T91I (n=3; MICs = 0.18-0.5 mg/L). The ciprofloxacin-resistant isolate with the highest ciprofloxacin MIC value (0.5 mg/L) also harboured a mutation in *parC* (D86N).

In July 2019 (outside the time period of this survey), additional ciprofloxacin-resistant isolates were received at the MRU (section 3.2).

Table 3-13: Characteristics of ciprofloxacin-resistant IMD isolates in England, Wales and Northern Ireland from 2010/11-2018/19.

ID	Epidemiological Year	Serogroup	Sequence type	Clonal complex	Ciprofloxacin MIC (mg/L)	*gyrA allele*	*gyrA* mutation[a]	*parC* allele	*parC* mutation[b]
63559	2018/ 2019	NG	14117	UA	0.06	296	D95N	928	None
35775	2014/ 2015	C	11	11	0.094	10	D95N	1	None
89259	2018/ 2019	B	230	32	0.18	8	T91I	1794	None
35789	2014/ 2015	B	8054	41/44	0.19	146	T91I	152	None
20338	2010/ 2011	A	4789	5	0.5	6	T91I	191	D86N

[a] ciprofloxacin resistance-associated mutation; [b] associated with enhanced ciprofloxacin MICS values; NG = Non-groupable

3.2 An outbreak of meningococcal disease owing to ciprofloxacin-resistant non-groupable ST-175 CC isolates in England, 2019.

Declaration: Much of the work described in this section (3.2) was published in Willerton et al., 2020. Excepting minor corrections from co-authors, the article was written solely by me.

Objective: Investigate ciprofloxacin resistance amongst isolates of the ST-175 CC, following an outbreak of meningococcal disease owing to ciprofloxacin-resistant NG ST-175 CC isolates in England, and to characterise the strain responsible in terms of population structure.

3.2.1 Outbreak details

In 2019, the MRU received isolates from invasive (n=1; 89713) and conjunctivitis (n=2; 89565, 89712) cases of meningococcal disease in England. The two conjunctivitis case isolates were from patients presenting with meningococcal disease upon return from travel to Mecca, KSA. The invasive isolate was from a complement deficient patient that attended the same mosque as one of the conjunctivitis cases. Following characterisation, all three isolates were NG belonging to ST-175 CC, ciprofloxacin-resistant (MICs = 0.125 mg/L) with reduced susceptibility to penicillin (MICs = 0.25 mg/L) (Denoted by * in Table 3-14, section 3.2.2.1).

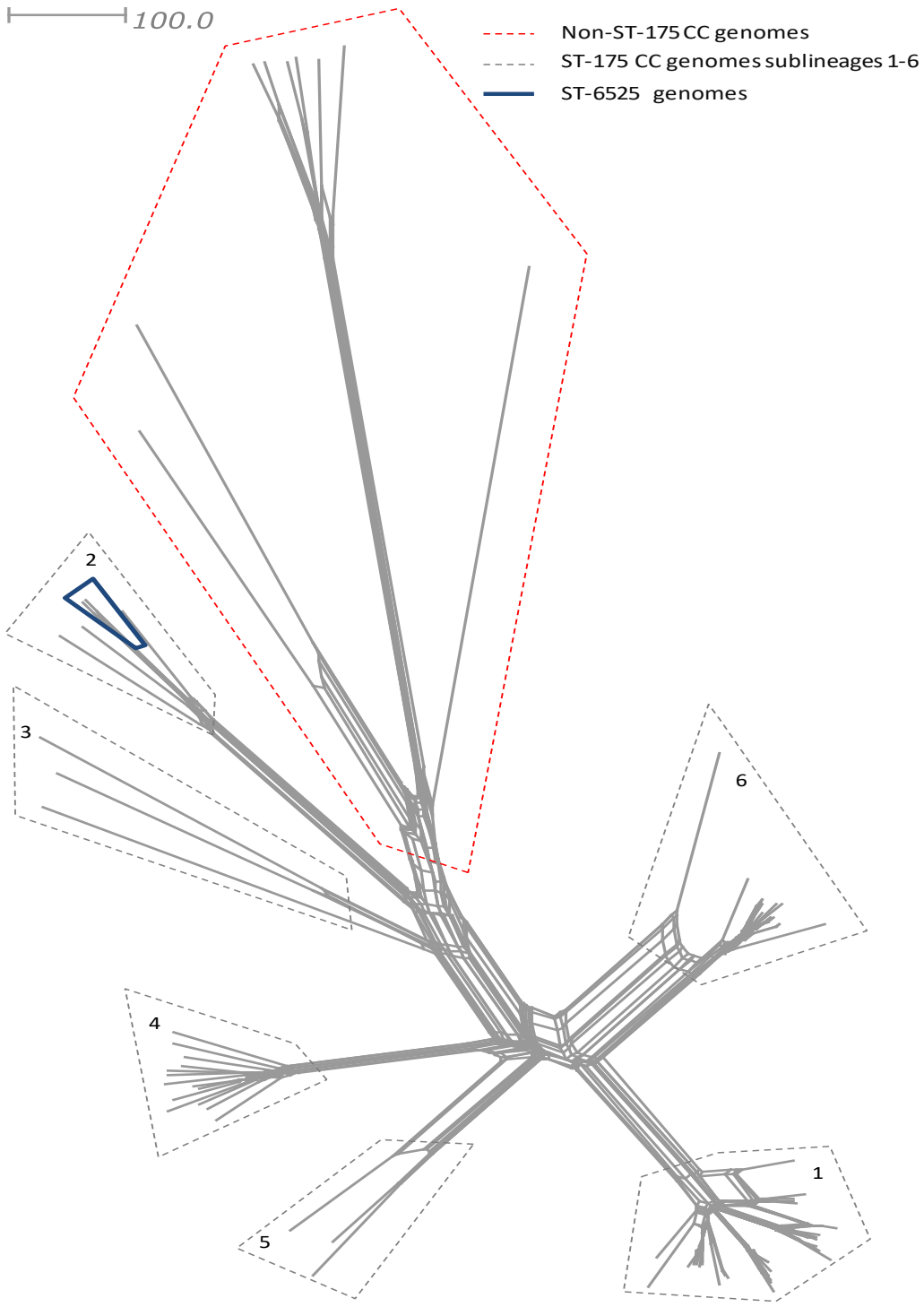
The outbreak led to the issue of a public health announcement (Public Health England, 2019) and subsequently the National Reference Centre for Meningococci and Haemophilus influenzae in Germany (Institute for Hygiene and Microbiology, University of Würzburg) highlighted four similar invasive cases caused by ST-175 CC isolates, two of which were also in complement deficient patients and one in a cancer patient. Three of the isolates were resistant to ciprofloxacin (MICs = 0.064-0.094 mg/L) and all four displayed reduced susceptibly or resistance to penicillin (MICs = 0.19-0.5 mg/L) (Denoted by # in Table 3-14,

section 3.2.2.1). Three of German IMD cases occurred in asylum seekers from Afghanistan (n=2) and Nigeria (n=1).

3.2.2 Phylogenetic analysis of the ST-175 clonal complex

To identify related isolates, all PubMLST isolates with genomes >2mb were identified (n=19,802; accessed 22/10/2019). ST-175 CC isolates (n=62), closely related isolates (non-ST-175 CC) sharing ≥ three ST-175 alleles and ST-175 CC isolates from published (n=5; (Bratcher et al., 2019)) and unpublished (n=1) UK carriage studies were identified (Appendix 2). All isolates underwent phylogenetic analysis (n=79; Figure 3-30). Most genomes fell into six sublineages (n=70, sublineages 1-6) which included ST-175 CC isolates (n=68) and 2 ST-6525 isolates unassigned to a CC. The remaining non-ST-175 CC isolates were not included in the rest of the analyses (n=9). Isolates in sublineages 1 to 6 were from 15 countries from 2000-2019, were of multiple serogroups and were invasive (n=32), carrier (n=20) and conjunctivitis (n=2). The remaining (n=16) had unknown disease status. The known English cluster isolates and similar German isolates were in sublineage 1.

Figure 3-30: ST-175 clonal complex and closely related genomes (Willerton et al., 2020).



A core genome comparison of 1605 loci among ST-175 clonal complex (n=68) isolates, ST-6525 (Unassigned clonal complex; n=2) isolates and closely related non-ST-175 clonal complex isolates (n=9). Sublineages 1-6 are indicated. The scale bar indicates variable loci among the 1605 that underwent the comparison. CC = clonal complex.

3.2.2.1 Sublineage 1: The non-groupable ST-175 clonal complex sublineage

Sublineage 1 (the NG ST-175 CC sublineage), comprised NG isolates (n=31; Table 3-14), including the known English invasive/conjunctivitis and German invasive case isolates. Four other IMD isolates from England (n=1; 2015), Italy (n=2; 2017-2018) and Sweden (n=1; 2016) were identified. Sublineage 1 included numerous clusters (clusters A-E) and a singleton (Figure 3-31).

The known English cases were in Cluster A, along with two of the known invasive German cases (one cancer patient, one immune status unknown patient) and two newly identified invasive isolates from Italy (immune status of patients unknown). Ciprofloxacin-resistant isolates in cluster A (three English isolates and one German isolate from a cancer patient) harboured *gyrA313* (MICs = 0.064-0.12 mg/L). *GyrA313* had six AASs when aligned to a WT *gyrA* allele (A69S, T91I, N103D, I111V, V120I, D210E; Appendix 22). The remaining Cluster A isolates were ciprofloxacin-susceptible (*GyrA12*; MICs = 0.003-0.006 mg/L). *GyrA12* had no AASs when aligned to a WT *gyrA* allele (Appendix 22).

Cluster B comprised the other known German case isolates (n=2; immunocompromised patients) and a newly identified Swedish invasive isolate (from a pregnant case). Isolates were ciprofloxacin-resistant (MICs = 0.094 mg/L; *gyrA187*). *GyrA187* had six AASs when aligned to a WT *gyrA* allele (T91I, N103D, I111V, V120I, V199I, D210E; Appendix 22).

Clusters C and D comprised carrier isolates with *gyrA12* and, where known, MICs were 0.002-0.004 mg/L. Cluster E isolates comprised carrier isolates with unknown ciprofloxacin MICs with *gyrA* alleles 152 (n=4) and 12 (n=1). *GyrA152* had one AAS when aligned to a WT *gyrA* allele (D95N; Appendix 22).

The singleton from England harboured *gyrA12* and was ciprofloxacin-susceptible (MIC = 0.004 mg/L).

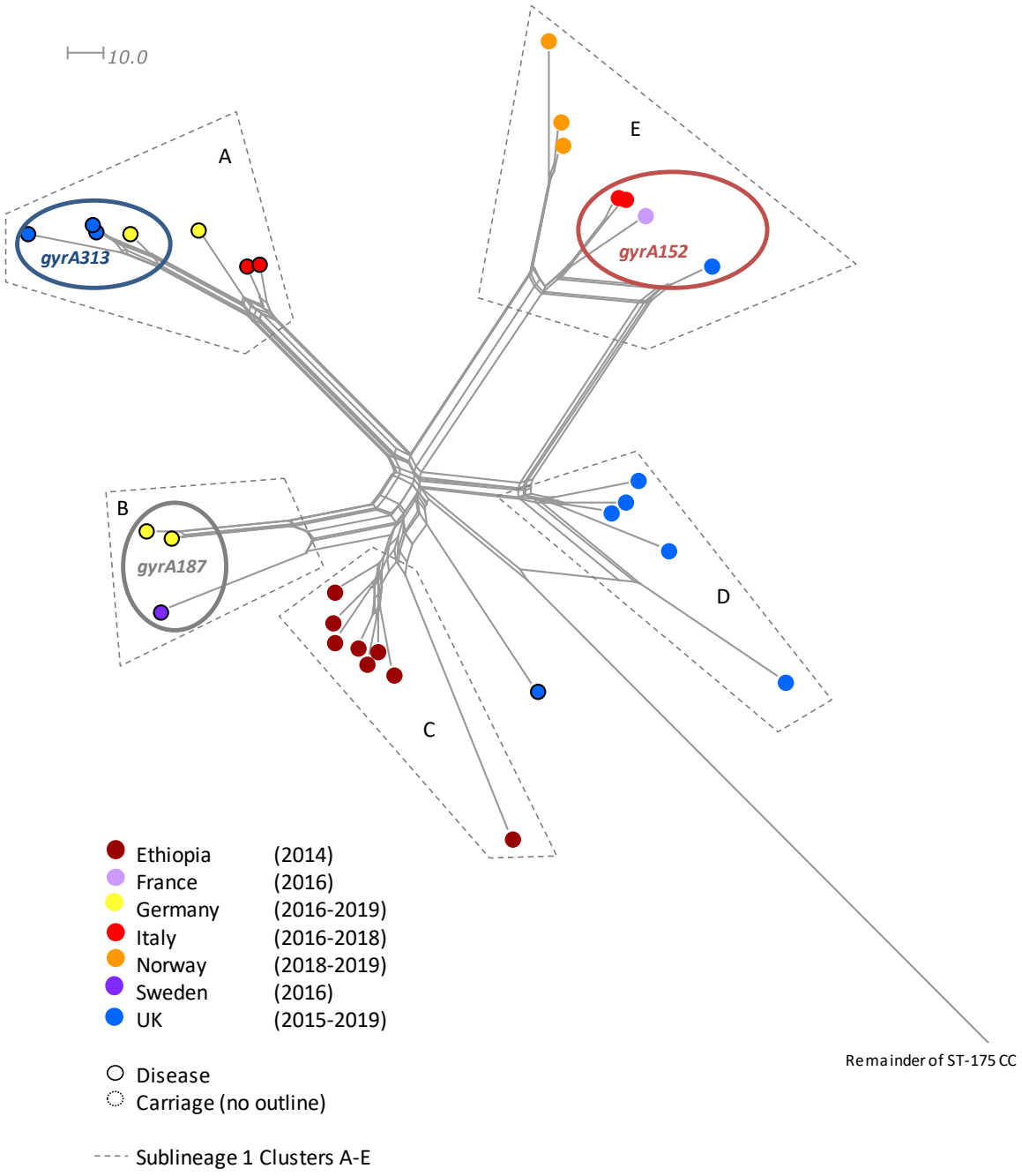
All isolates in sublineage 1 had *penA* alleles 662 (n=29) or 909 (n=2) and where MICs were known were PenR (n=1; 0.5 mg/L) and PenI (n=17; 0.094-0.25 mg/L). All isolates in Sublineage 1 harboured *ParC583*.

Table 3-14: Sublineage 1 isolates: the non-groupable ST-175 clonal complex sublineage isolates (Willerton et al., 2020).

Cluster	PubMLST ID	Year	Country	Disease	Immunocomprimised? (If invasive)	*gyrA* allele	Ciprofloxacin MIC (mg/L)	*penA allele*	Penicillin MIC (mg/L)	*PorA* VR2	fHbp variant	fHbp peptide	NHBA peptide
A	93631#	2017	Germany	Invasive	NK	12	0.003	662	0.25	15-25	1	321	9
	84075	2017	Italy	Invasive	NK	12	0.004	662	0.125	15-25	1	321	9
	91539	2018	Italy	Invasive	NK	12	0.006	662	0.25	15-25	1	321	9
	89565*	2019	UK	Conjunctivitis	n/a	313	0.12	662	0.25	15-25	3	111	9
	89712*	2019	UK	Conjunctivitis	n/a	313	0.12	662	0.25	15-25	3	111	9
	89713*	2019	UK	Invasive	Complement deficiency	313	0.12	662	0.25	15-25	3	111	9
	93679#	2019	Germany	Invasive	Plasmacytoma	313	0.064	662	0.19	15-25	3	111	9
B	93629#	2016	Germany	Invasive	Terminal complement deficiency	187	0.094	909	0.25	15-25	2	151	9
	93630#	2016	Germany	Invasive	Terminal complement deficiency	187	0.064	909	0.5	15-25	2	151	9
	42784	2016	Sweden	Invasive	Pregnant	187	0.094	662	0.094	15-25	2	151	9
C	41896[c]	2014	Ethiopia	Carrier	n/a	12	0.004	662	0.25	15-56	2	151	1578[b]
	41897[c]	2014	Ethiopia	Carrier	n/a	12	0.004	662	0.25	15-56	2	151	1578[b]
	42666[d]	2014	Ethiopia	Carrier	n/a	12	0.004	662	0.25	15-56	2	151	9
	42668[d]	2014	Ethiopia	Carrier	n/a	12	0.002	662	0.25	15-56	2	151	9
	60134	2014	Ethiopia	Carrier	n/a	12	0.002	662	0.25	15-25	2	151	9
	60143	2014	Ethiopia	Carrier	n/a	12	0.004	662	0.25	15-56	2	151	9
	60308	2014	Ethiopia	Carrier	n/a	12	0.002	662	0.125	15-56	2	151	9
	61207	2014	Ethiopia	Carrier	n/a	12	NK	662	NK	15-56	2	151	9
D	49960	2015	UK	Carrier	n/a	12	NK	662	NK	15-25	2	151	9
	50082	2015	UK	Carrier	n/a	12	NK	662	NK	15-25	2	151	9
	52614	2015	UK	Carrier	n/a	12	NK	662	NK	15-25	2	151	9
	52715	2015	UK	Carrier	n/a	12	NK	662	NK	15-25	2	151	9
	88632	2018	UK	Carrier	n/a	12	NK	662	NK	15-25	2	151	9
E	52572	2015	UK	Carrier	n/a	152	NK	662	NK	15-25	1	321	9
	41727	2016	France	Carrier	n/a	152	0.125	662	NK	15-25	1	321	9
	47101	2016	Italy	Carrier	n/a	152	NK	662	NK	15-25	1	321	9
	47115	2016	Italy	Carrier	n/a	152	NK	662	NK	15-25	1	321	9
	84968	2018	Norway	Carrier	n/a	12	NK	662	NK	15-25	1	321	9
	85033	2018	Norway	Carrier	n/a	12	NK	662	NK	15-25	1	321	9
	92641	2019	Norway	Carrier	n/a	12	NK	662	NK	15-75	1	321	9
S[a]	41526	2015	UK	Invasive	No[e]	12	0.004	662	0.19	15-25	2	151	9

All isolates had allele 583 for *parC* and allele 311 for *nadA*. [a]Singleton. [b]nhba allele had 1 bp different from allele 7.[c/d] Isolates both from same person 8 weeks difference. [e] complement deficiencies due to vasculitis and Eculizumab therapy, splenic dysfunction, HIV, glomerulonephritis, asplenia plus inherited deficiencies were ruled out. NK = not known. *English outbreak isolates. #German isolates similar to English outbreak isolates.

Figure 3-31: Isolates belonging to Sublineage 1 - the non-groupable ST-175 clonal compelx sublineage (Willerton et al., 2020).

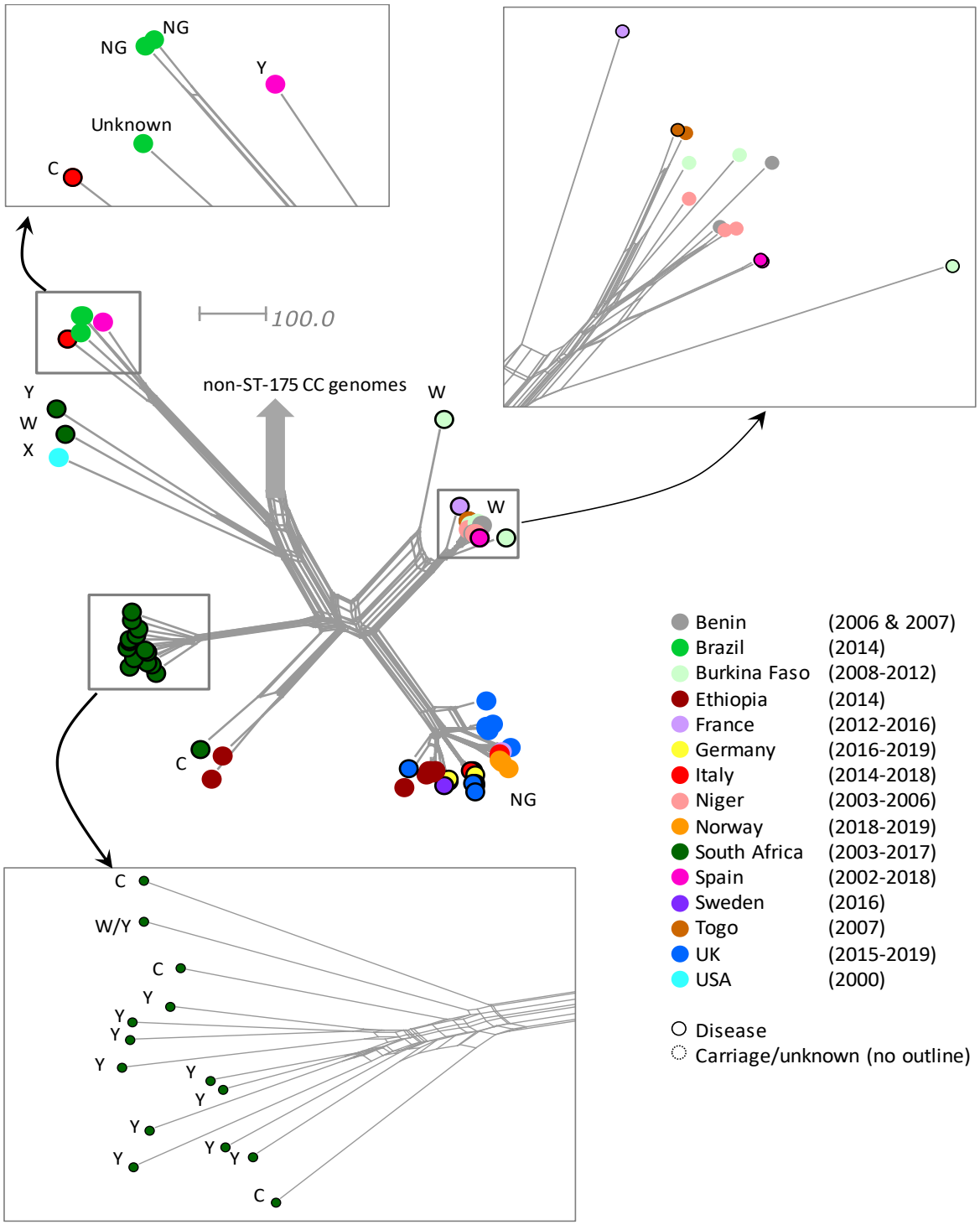


Core genome comparison based on 1605 loci among Sublineage 1 isolates of ST-175 clonal complex (n=31). The sublineage comprised clusters A-E (indicated) and a singleton. The scale bar indicates variable loci among the 1605 that underwent the comparison. Isolate 40593 was the reference strain (to remainder of ST-175 clonal complex). CC = clonal complex.

3.2.2.2 Sublineages 2-6

Isolates in sublineages 2 to 6 (n=39) comprised invasive isolates (n=23) and those with unknown disease state (n=16) from 2000-2018 (Figure 3-32). They were from 10 different countries and were serogroup W (n=15), Y (n=12), C (n=7), NG (n=2), W/Y (n=1) and X (n=1). The serogroup was unknown for one isolate. All isolates harboured *gyrA12* (Appendix 2).

Figure 3-32: ST-175 clonal complex and ST-6525 isolates from 2000-2019 (Willerton et al., 2020).



Core genome comparison based on 1605 loci among ST-175 clonal complex (n=68), ST-6525 (n=2) and non-ST-175 clonal complex isolates (n=9, not shown). The scale bar indicates variable loci among the 1605 that underwent the comparison. CC = clonal complex.

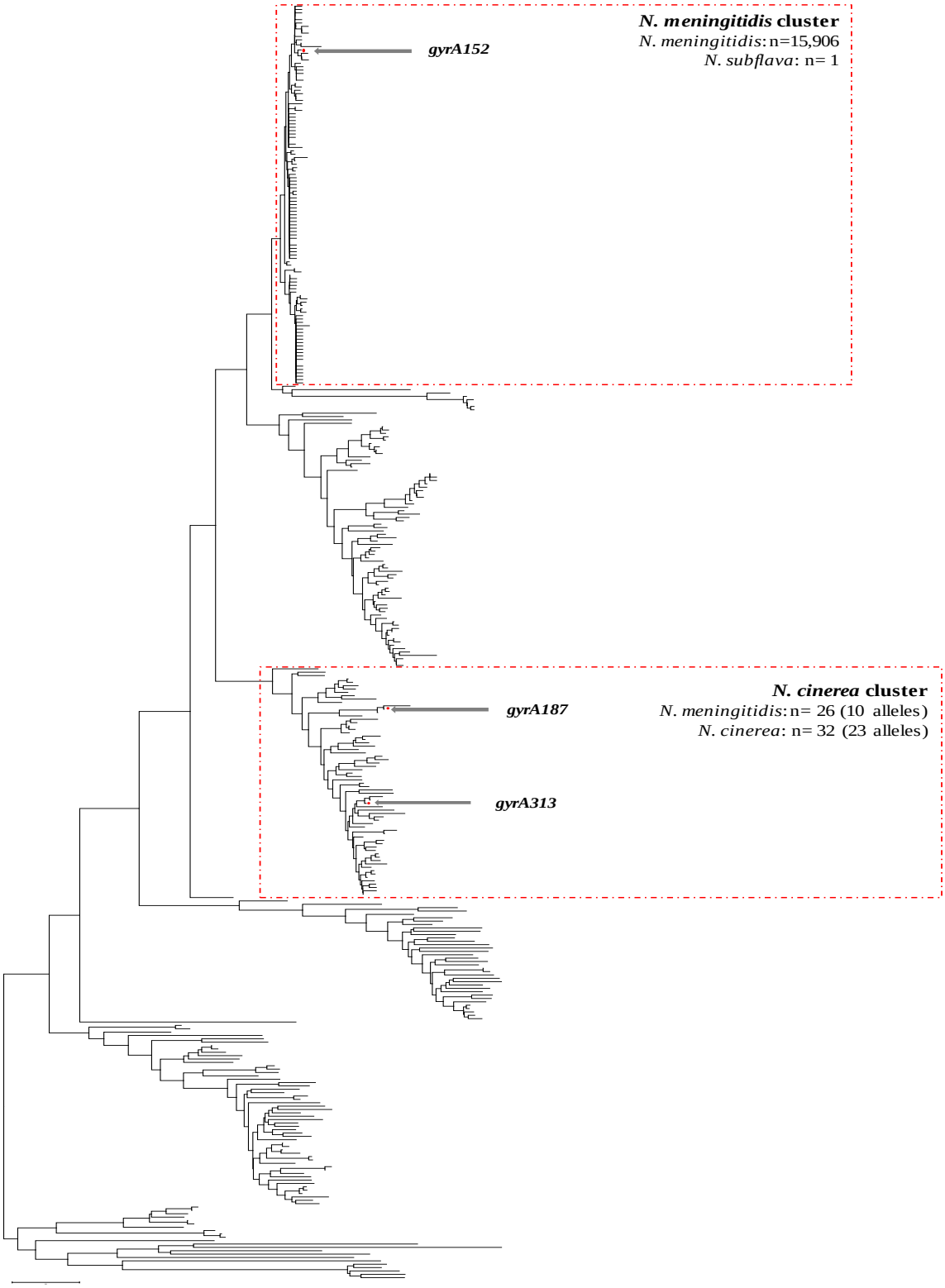
3.2.3 Origins of ciprofloxacin-resistant determinants

On an alignment with all known *gyrA* alleles, the *gyrA* alleles identified in Sublineage 1 – the non-groupable ST-175 CC sublineage that had AASs when aligned to a WT *gyrA* allele (*gyrA313*, *gyrA187* and *gyrA152*) belonged to two clades associated with *N. meningitidis* and *N. cinerea* (Figure 3-33). The *N. cinerea* cluster contained *gyrA313* and *gyrA187* (found in invasive and conjunctivitis case isolates) while the *N. meningitidis* clade contained *gyrA152* (found only among carrier isolates).

3.2.4 Potential vaccine coverage of the non-groupable ST-175 clonal complex sublineage isolates

All isolates in Sublineage 1 had *NadA311* which contained an insertion sequence (IS1301) rendering it non-expressible. PorA P1.4 was not expressed by any of the isolates. All the isolates possessed peptides 9 (n=29) or 1578 (n=2) NHBA alleles. FHbp variant 1 allele (peptide 321) was harboured by 10 isolates which included three invasive isolates. FHbp variant 2 and 3 alleles were harboured by the remaining isolates: peptide 151 (n=17) and peptide 111 (n=4), respectively.

Figure 3-33: Phylogenetic analysis of all *gyrA* alleles and species distribution on PubMLST (Willerton et al., 2020).



Neighbor-Joining tree of nucleotide sequences of available PubMLST *gyrA* alleles (n=379; accessed 13/05/2020). Altered *gyrA* alleles among sublineage 1 isolates (alleles 152, 187 and 313) are highlighted. MEGA4 was used to construct the tree. The number of nucleotide differences is represented by the scale bar.

3.3 Penicillin resistance among English invasive meningococcal serogroup W ST-11 clonal complex isolates, July 2010-August 2019.

Declaration: Much of the work described in this section (3.3) was published in Willerton et al., 2021. Excepting minor corrections from co-authors, the article was written solely by me.

Objective: Investigate the observed increase in penicillin resistance among English serogroup W ST-11 CC IMD isolates received at the MRU in 2018 and identify closely related isolates on the PubMLST database.

3.3.1 English invasive (MGL) serogroup W ST-11 clonal complex isolates

In order to identify all English invasive serogroup W ST-11 CC and closely related MenW IMD isolates from July 2010, MLST data for all genomes available on the MGL database were exported (n=4,781, accessed 01/05/2020). Non-English genomes (n=826), followed by non-serogroup/genogroup W genomes (n=2,976), non-ST-11 CC genomes (n=69) and genomes with < four ST-11 MLST alleles (n=13) were removed from the dataset. The remaining genomes (n=897; Appendix 1 and 3), included English invasive serogroup W ST-11 CC genomes (n=867) and closely related English invasive serogroup W ST-11 CC genomes with incomplete MLST profiles with four or more ST-11 MLST alleles (n=30).

3.3.1.1 Distribution of penicillin resistance among English invasive serogroup W ST-11 clonal complex isolates

Between July 2010 and August 2019, 897 English invasive ST-11 CC isolates were identified (section 3.3.1). Seven hundred and sixteen were PenS (80%; MICs = 0.004-0.064 mg/L), 156 were PenI (17%; MICs = 0.094-0.25 mg/L) and 25 were PenR (3%, MICs = 0.038-0.75 mg/L). Twelve out of the 25 PenR isolates were received at the MRU in 2018 alone (Table 3-15).

Table 3-15: Distribution of penicillin susceptibility among English invasive serogroup W ST-11 clonal complex isolates from July 2010-August 2019.

	Number of English serogroup W ST-11 CC Isolates (%)			
Year	**PenS ≤0.06 mg/L**	**PenI 0.094-0.25 mg/L**	**PenR >0.25 mg/L**	**Total**
July – December 2010	2 (50)	1(25)	1(25)	4
2011	11 (84.6)	2 (15.4)	0	13
2012	21(91.30)	1 (4.35)	1 (4.35)	23
2013	46 (79.3)	11 (19.0)	1 (1.7)	58
2014	83 (88.3)	11(11.7)	0	94
2015	123 (76.4)	37 (23.0)	1 (0.6)	161
2016	134 (76.6)	39 (22.3)	2 (1.1)	175
2017	145 (86.8)	20 (12.0)	2 (1.2)	167
2018	107 (81.1)	13 (9.8)	12 (9.1)	132
January – August 2019	44 (62.9)	21 (30.0)	5 (7.1)	70

PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines. CC = clonal complex.

Five *penA* alleles (alleles 9, 14, 171, 435 and 540) were identified among the 25 English invasive PenR serogroup W ST-11 CC isolates, and all but one allele (*penA171*) contained the five AASs conferring reduced susceptibility or resistance to penicillin (Table 3-16). An investigation into *penA171* and the respective isolate was performed (section 3.1.2.5). Eight *penA* alleles were identified among the 156 PenI isolates (Table 3-16).

Table 3-16: *PenA* alleles among English invasive PenR and PenI serogroup W ST-11 clonal complex isolates.

	Number of serogroup W ST-11 CC Isolates			
***PenA* allele**	**Total**	**PenI (MIC mg/L)**	**PenR (MIC mg/L)**	**Number of AASs associated with conferring reduced susceptibility or resistance to penicillin (F504L, A510V, I515V, H541N, I566V)**
9	25	7 (0.19-0.25)	18 (0.38-0.75)	5
14	18	15 (0.125-0.25)	3 (0.38-0.5)	5
540	2		2 (0.38)	5
435	1		1 (0.38)	5
171	1		1 (0.38)	0
1	125	125 (0.094-0.25)		0
90	5	5 (0.125-0.19)		5
62	1	1 (0.094)		0
315	1	1 (0.25)		5
625	1	1 (0.19)		5
935	1	1 (0.19)		5

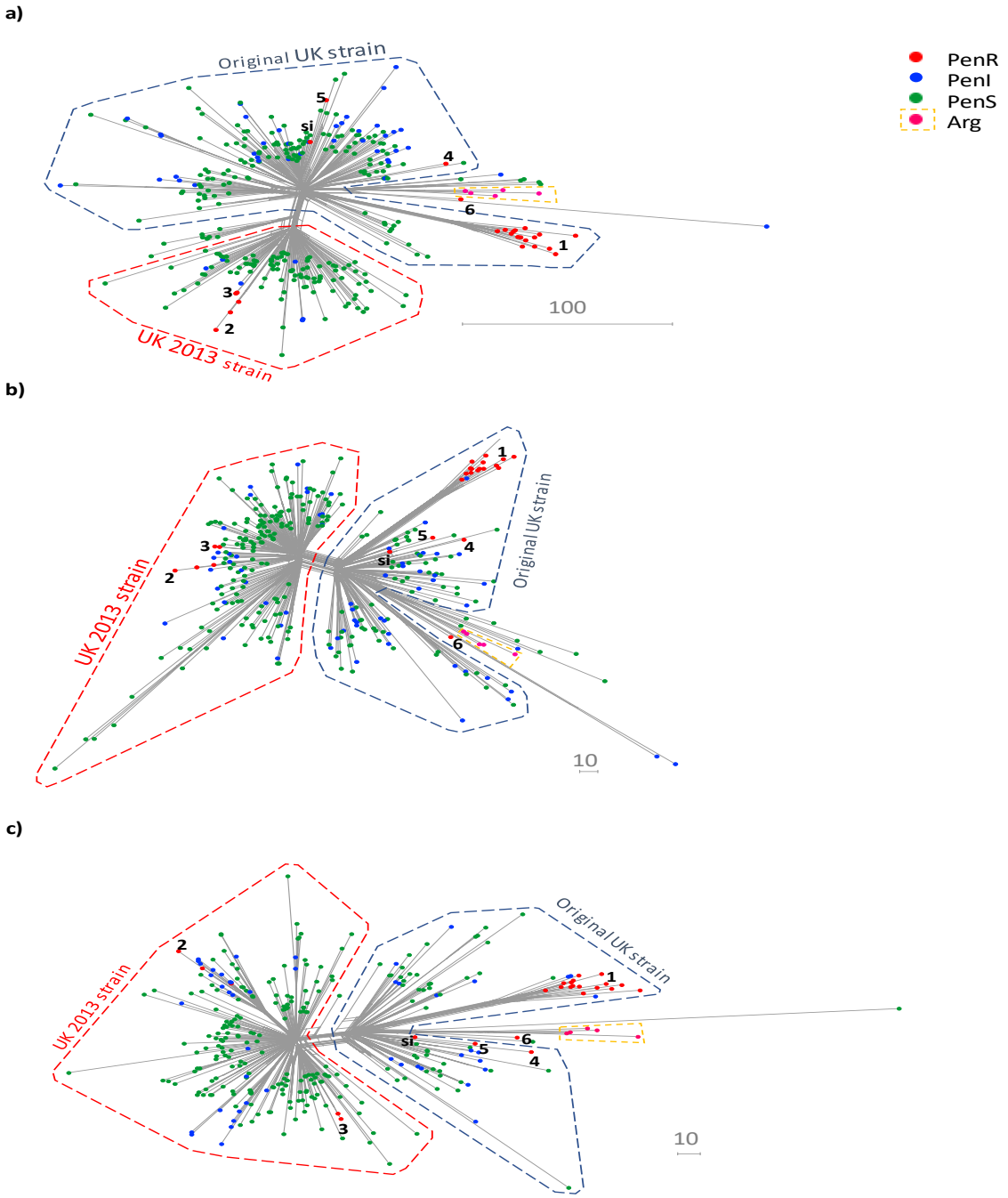
PenS = Penicillin-susceptible, standard exposure; PenI = Penicillin-susceptible, increased exposure; PenR = Penicillin-resistant according to EUCAST guidelines. AASs = amino acid substitutions.

The genomes of all English invasive serogroup W ST-11 CC isolates (n=897) were split into three manageable groups (a-c; Figure 3-34), each containing the genomes of the 25 PenR isolates, which underwent phylogenetic analysis with Argentinian South American reference genomes (n=5; 31148, 31149, 31150, 31151, 31152).

Genomes of English invasive PenS and PenI serogroup W ST-11 CC isolates were widely distributed throughout the population. The English invasive PenR serogroup W ST-11 CC isolates belonged to six distinct lineages (penicillin resistance-associated lineages 1-6) and one was a singleton (Appendix 23) (Willerton et al., 2021).

Penicillin resistance-associated lineages 1, 4, 5 and the singleton belonged to the original UK strain. Penicillin resistance-associated lineages 2 and 3 were of the UK 2013 strain whilst penicillin resistance-associated lineage 6 belonged to the South American strain.

Figure 3-34: Penicillin susceptiblity of English invasive serogroup W ST-11 clonal complex isolates, July 2010-August 2019 (Willerton et al., 2021).



Core genome comparison of 1605 core genome loci among English invasive serogroup W ST-11 complex isolates (n=897). Genomes divided into three groups: a) July 2010-September 2015, b) September 2015-April 2017 and c) April 2017-August 2019. Each network contains PenR English invasive serogroup W ST-11 clonal complex isolates (n=25) and South American reference genomes (Arg n=5); PubMLST IDs 31148, 31149, 31150, 31151, 31152). The number of variable loci among the 1605 that were compared is represented by the scale bar. PenR = penicillin-resistant, PenI = penicillin-susceptible, increased exposure, PenS = penicillin-susceptible, standard exposure. Penicillin resistance-associated lineages 1-6 labelled. si = singleton.

3.3.2 Non-invasive English and rest of the world (non-MGL) serogroup W ST-11 clonal complex isolates

In order to identify all other (non-invasive English and rest of the world) serogroup W ST-11 CC and closely related MenW isolates, MLST data for all available genomes on the PubMLST database (>1 Mb of sequence data) were exported (n=22,918; accessed 01/05/2020). Non-meningococcal genomes (n=5,162), followed by non-ST-11 CC genomes (n=11,440), non-MenW genomes (n=1,798; genogroup annotation given priority over serogroup), poor quality genomes (n=20; <2Mb and/or >1000 contigs) and genomes with < four ST-11 MLST alleles (n=1,387) were removed from the dataset. The English invasive serogroup W ST-11 CC isolates (n=897; section 3.3.2) were also removed. The remaining genomes (n=2,214) were serogroup W ST-11 CC isolates (n=2,197) and closely related serogroup W ST-11 CC genomes with incomplete MLST profiles with four or more ST-11 MLST alleles (n=17).

3.3.2.1 Non-MGL isolates closely related to English invasive penicillin-resistant serogroup W ST-11 clonal complex isolates

To firstly identify genomes of non-MGL serogroup W ST-11 CC isolates of the original UK and UK 2013 strains, genomes (n=2,214; section 3.3.3), were split into eight manageable groups and underwent phylogenetic analysis with the Argentinian South American strain reference genomes (n=5) and an Original UK strain reference genome (30154) (Appendix 24).

To identify those belonging to any of the penicillin-resistant associated lineages previously identified (1-6; section 3.3.2), non-MGL genomes of the Original UK and Original 2013 (n=1,152) were split into four manageable groups (a-d; Figure 3-35) and each underwent phylogenetic analysis with the English invasive PenR serogroup W ST-11 CC genomes (n=25) and South American strain reference genomes (n=5). One hundred and thirty-one non-MGL serogroup W ST-11 CC genomes belonged to penicillin resistance-associated lineages 1 to 6 (Appendix 23).

Figure 3-35: Non-MGL serogroup W isolates of ST-11 clonal complex of South American sublineage belonging to the English penicillin resistance-associated lineages (Willerton et al., 2021).

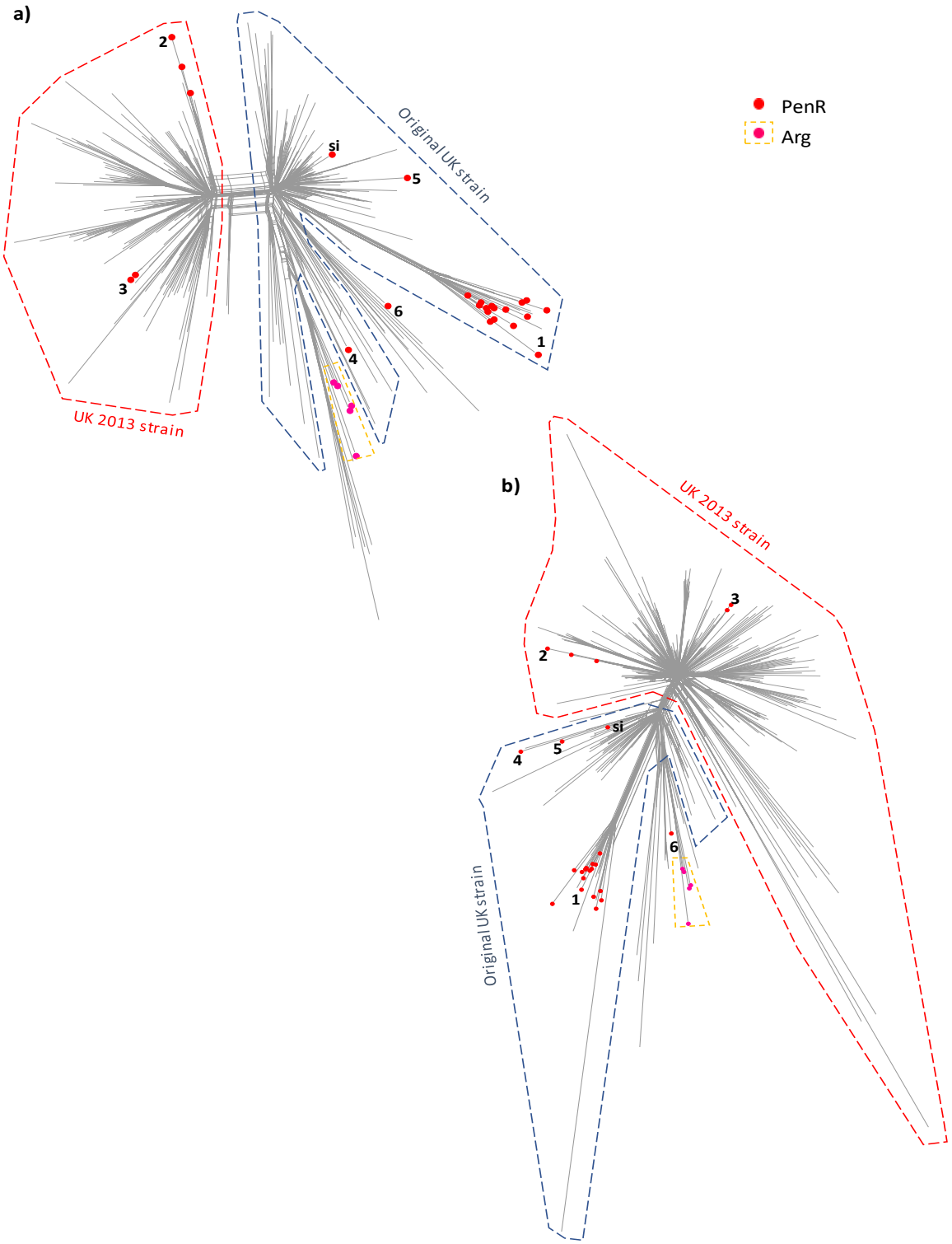
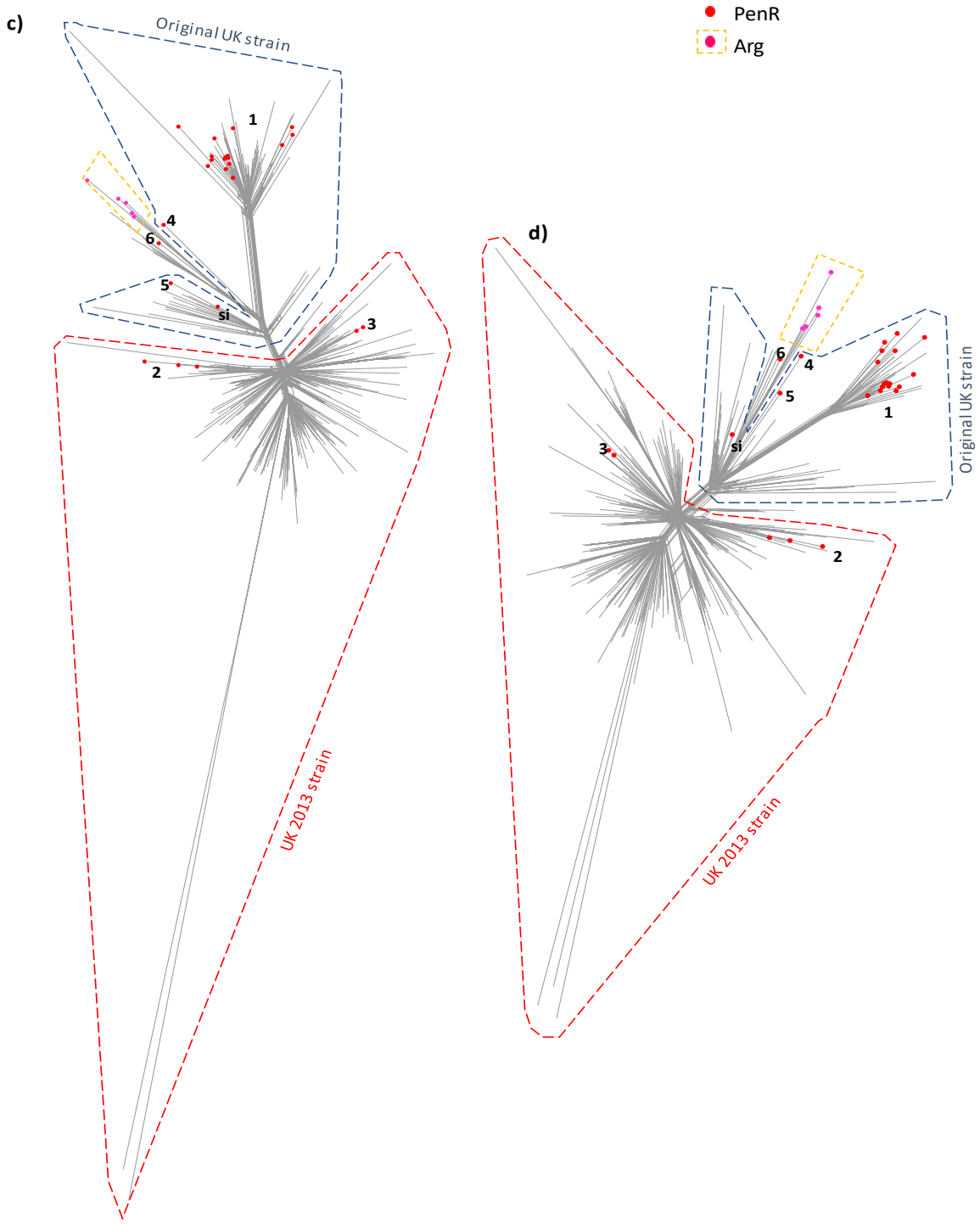


Figure 3-35 (continued).



Core genome comparison of 1605 core genome loci of English penicillin-resistant invasive serogroup W ST-11 clonal complex isolates (n=25) and non-MGL serogroup W ST-11 complex isolates (n=2,214; English invasive isolates removed). The non-MGL genomes split into groups labelled a-d. Each network contains English penicillin-resistant invasive serogroup W ST-11 complex isolates (PenR; n=25) and South American reference isolates (Arg; n=5).

3.3.3 The penicillin resistance-associated lineages

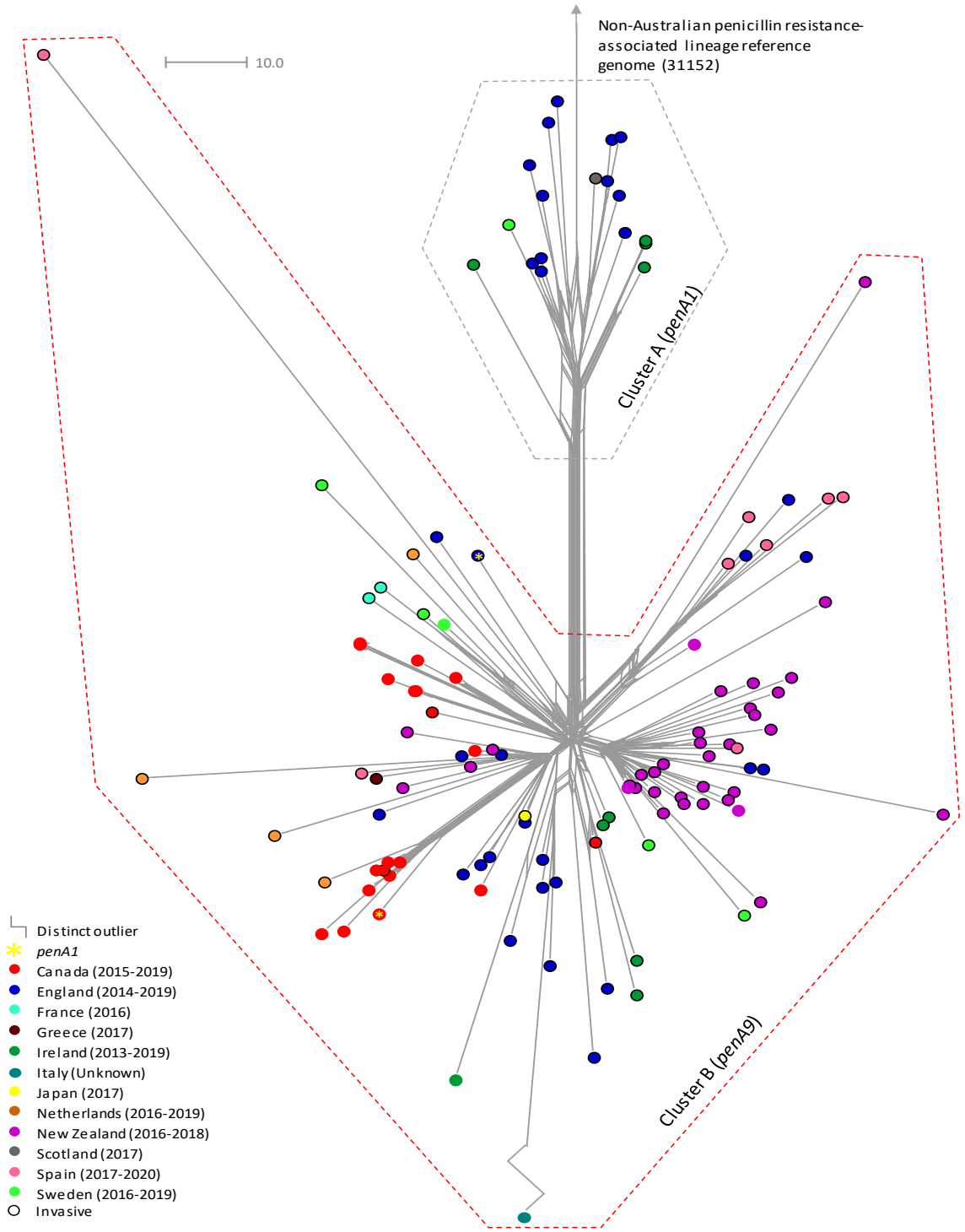
3.3.3.1 Penicillin resistance-associated lineage 1 – The Australian penicillin resistance-associated lineage

Penicillin resistance associated lineage 1, termed the Australian penicillin resistance-associated lineage, included n=122 isolates, counting those PenR serogroup W ST-11 CC isolates previously reported by Mowlaboccus and colleagues in 2016 (n=5) (Mowlaboccus et al., 2017).

Genomes of isolates in the Australian penicillin resistance-associated lineage underwent phylogenetic analysis which revealed two separate clusters (A and B; Figure 3-36). Cluster A comprised n=18 genomes of isolates from England (n=12; 2014-2018), Ireland (n=4; 2013-2015), Scotland (n=1; 2017) and Sweden (n=1; 2018). All genomes in cluster A harboured *penA1* and where MIC data were available were PenS (n=10; MICs = 0.032-0.64 mg/L) or PenI (n=2; MICs = 0.094-0.125 mg/L).

Cluster B comprised n=104 genomes of isolates from New Zealand (n=35; 2016-2018), Canada (n=21; 2015-2019), England (n=21; 2016-2019), Spain (n=8; 2017-2020), Ireland (n=5; 2017-2019), Sweden (n=5; 2016-2019), the Netherlands (n=4; 2016-2019), France (n=2; 2016), Greece (n=1; 2017), Italy (n=1; unknown) and Japan (n=1; 2017). Ninety-eight percent of cluster B genomes (n=102) harboured *penA9* and for those with known MICs were PenR (n=35; MICs = 0.38-1.0 mg/L), PenI (n=19; 0.19-0.25 mg/L) or PenS (n=1; MIC = 0.03 mg/L). Sixty-eight percent of Cluster B isolates (n=71) were identified in 2017 and 2018 (Appendix 25).

Figure 3-36: Serogroup W ST-11 clonal complex isolates of penicillin resistance-associated lineage 1 (Willerton et al., 2021).



Core genome comparison based on 1605 core genome loci of serogroup W ST-11 complex isolates belonging to penicillin resistance-associated Lineage 1 (n=122). The number of variable loci among the 1605 compared is represented by the scale bar.

3.3.3.2 Penicillin resistance-associated lineage 2 – The UK 2013 penicillin resistance-associated lineage

Penicillin resistance-associated lineage 2, termed the UK 2013 penicillin resistance-associated lineage, contained n=62 genomes which underwent phylogenetic analysis to reveal two separate clusters (clusters A and B; Figure 3-37).

Cluster A contained n=49 genomes from England (n=25; 2016-2019), Germany (n=6; 2018-2019), Scotland (n=4; 2017-2020), Ireland (n=3; 2017-2018), the Netherlands (n=3; 2016-2018), Wales (n=3; 2016-2019), France (n=1; 2018), Northern Ireland (n=1; 2016), Portugal (n=1; 2019), Spain (n=1; 2019) and Sweden (n=1; 2018). All genomes in Cluster A possessed *penA1* and where MICs were known, isolates were PenS (n=23; MICs = 0.047-0/064mg/L) or PenI (n=6; MICs = 0.094 mg/L).

Cluster B comprised n=13 genomes from England (n=11; 2017-2019), Scotland (n=1; 2019) and Sweden (n=1; 2018). All genomes harboured *penA14* and where MICs were known were PenR (n=3; MICs = 0.38-0.5 mg/L) or PenI (n=8; MICs = 0.25 mg/L). Sixty-nine percent of cluster B isolates (n=9) were identified in 2019 alone (Appendix 26).

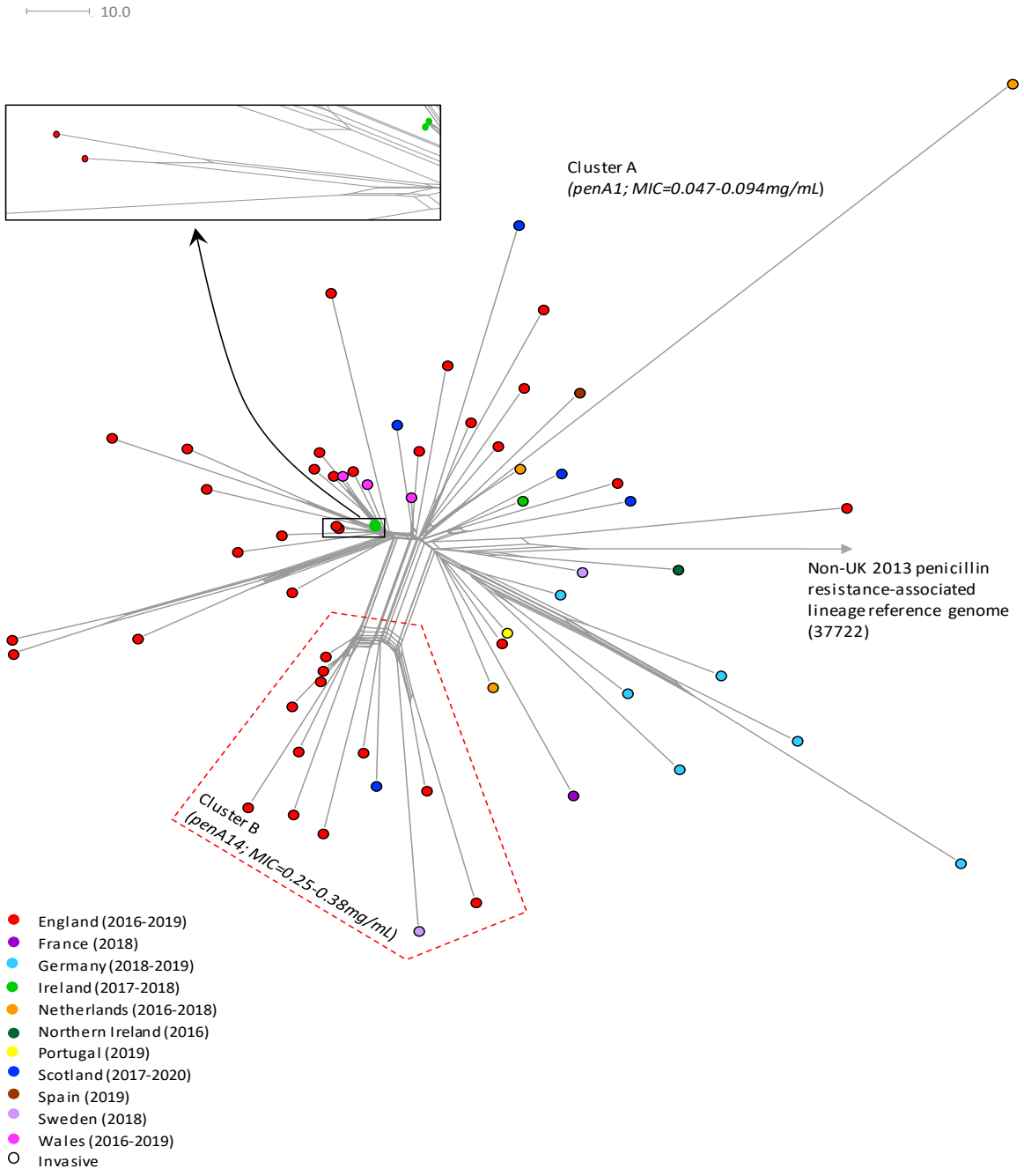
3.3.3.3 Penicillin resistance-associated lineage 3

Penicillin resistance-associated lineage 3, belonging to the UK 2013 strain, comprised n=4 genomes from England (n=2; 2018-2019), Spain (n=1; 2017) and Scotland (n=1; 2020). The English genomes harboured *penA540* and were PenR (MICs = 0.38 mg/L). The remaining genomes harboured *penA1* (MICs unknown).

3.3.3.4 Penicillin resistance-associated lineage 4, 5, 6 and the singleton

Penicillin resistance-associated lineages 4, 5 and 6 (comprised n=12, n=2 and n=10 isolates respectively) contained one PenR isolate each from England (*penA9, penA435 and penA9*, respectively; MIC = 0.38 mg/L) together with isolates harbouring *penA1* (MICs = 0.006 – 0.125 mg/L). The English singleton was PenR (MIC = 0.38 mg/L) harbouring *penA171*.

Figure 3-37: Serogroup W ST-11 clonal complex isolates of penicillin resistance-associated lineage 2 (Willerton et al., 2021).



Core genome comparison of 1605 core genome loci of serogroup W ST-11 clonal complex isolates of penicillin resistance-associated lineage 2 (n=62). The number of variable loci among the 1605 compared is represented by the scale bar.

3.3.3.5 Species distribution of *penA* alleles identified among English penicillin-resistant serogroup W ST-11 clonal complex isolates

PubMLST genomes that had any of the *penA* alleles harboured by the English PenR serogroup W ST-11 CC isolates were identified (Table 3-17; *penA14*, n=1,099; *penA9*, n=763; *penA540*, n=18; *penA171*, n=8; *penA435*, n=1; accessed 12/06/2020). *PenA540* and *penA435* were found among meningococcal isolates only (n=18 and n=1 respectively). *PenA9* was found among *N. meningitidis* (n=705), *N. gonorrhoeae* (n=37), *N. lactamica* (n=13), *N. polysaccharea* (n=4), *N. cinerea* (n=3) and *N. bergeri* (n=1). *PenA14* was found among *N. meningitidis* and *N. gonorrhoeae* isolates (n=1,085 and n=14, respectively) as was *penA171* (n=6 and n=2, respectively) (Willerton et al., 2021).

Table 3-17: PubMLST *Neisseria* isolates possessing *penA* alleles identified among English penicillin-resistant invasive serogroup W ST-11 clonal complex isolates (Willerton et al., 2021).

***PenA* allele**	**Total**	***N. bergeri***	***N. cinerea***	***N. gonorrhoeae***	***N. lactamica***	***N. polysaccharea***	***N. meningitidis***	**Clonal complexes of *N. meningitidis* isolates**
9	763	1	3	37	13	4	705	ST-11 (n=158), ST-32 (n=108), ST-198 (n=85), UA (n=55), NK (n=50), ST-865 (n=45), ST-41/44 (n=36), ST-23 (n=32), ST-213 (n=24), Incomplete MLST (n=10), Other (n=102)
14	1099			14			1085	ST-22 (n=372), ST-269 (n=182), ST-41/44 (n=88), UA (n=98), NK (n=81), ST-213 (n=43), ST-162 (n=41), ST-11 (n=34), ST-1157 (n=25), Incomplete MLST (n=24), ST-60 (n=23), Other (n=74)
171	8			2			6	ST-865 (n=2), ST-103 (n=1), ST-11 (n=1), ST 41/44 (n=1), UA (n=1)
435	1						1	ST-11 (n=1)
540	18						18	UA (n=14), ST-11 (n=2), ST-269 (n=1), Incomplete MLST (n=1)

UA = unassigned. NK = not known.

4 Discussion

Except for sulphonamides, *N. meningitidis* has remained largely susceptible to the antibiotics used for treatment and prophylaxis of IMD. Resistance to 3GCs, ceftriaxone and cefotaxime, among meningococci are seldom reported, with only one study having reported this thus far (Manchanda and Bhalla, 2006). However, a lack of adequate strain characterisation has cast doubt among concerned researchers (Nicolas, 2007), whose calls for further testing of the isolates are yet to be answered. Ciprofloxacin resistance among meningococci had been sporadically reported across the globe, apart from in China, where it is highly prevalent (Zhu et al., 2014). Rifampicin resistance is uncommon in meningococci isolated from index cases and is more frequently reported amongst those from close contacts, where rifampicin has previously been used for chemoprophylaxis. Reduced susceptibility and resistance to penicillin among meningococci is becoming increasingly reported across the globe, due to alterations within the *penA* gene (Bowler et al., 1994).

In the UK, the MRU has been performing AST on all IMD isolates alongside WGS of isolates since July 2010. Analysis of the data had not been undertaken prior to this project, and therefore the distribution of ABR among IMD isolates in the UK is currently unknown.

The aim of this project was to analyse MIC values (penicillin, rifampicin, ciprofloxacin and cefotaxime) and WGS data for all isolates from culture-confirmed cases of IMD in England, Wales and Northern Ireland from July 2010 to June 2019. Further aims were to investigate an observed increase in IMD caused by penicillin-resistant serogroup W ST-11 CC isolates and to investigate a recent outbreak of meningococcal disease caused by ciprofloxacin-resistant NG isolates.

From July 2010 to June 2019, the MRU received 4,122 IMD isolates for which WGS data was obtained.

4.1 Penicillin susceptibility among IMD isolates in England, Wales and Northern Ireland

Out of the 4,122 IMD isolates received at the MRU from July 2010 to June 2019, 113 were PenR (MICs = 0.38-0.75 mg/L). Sixty-four were serogroup B, 25 were serogroup W, 13 were serogroup C, nine were serogroup Y, one was serogroup W/Y and one was NG. Prior to 2015/16, the annual proportion of PenR isolates was always less than or equal to 2%, however has been greater than 3% in each subsequent year, with the highest proportion of PenR isolates observed in 2018/19 (7%). This was largely due to an increase in the number of PenR isolates received and suggests that, as has been reported in other countries, penicillin resistance among meningococci is increasing gradually with time (Bertrand et al., 2012; Mowlaboccus et al., 2017; Vacca et al., 2018).

Amongst the PenR isolates, an increase in the number of Serogroup W ST-11 CC isolates was observed over recent years, particularly since 2018. From July 2010 to August 2019, 25 English MenW ST-11 CC PenR isolates were received at the MRU; 17 of these were received from January 2018 – August 2019 alone. After an outbreak of MenW disease following a Hajj pilgrim in 2000, MenW disease has increased globally (Abad et al., 2014; Mustapha et al., 2016; Knol et al., 2017). In 2009, MenW disease in England began to increase, mainly due to the expansion of two strains, the Original UK and UK 2013 strains, that descended from a South American strain (Lucidarme et al., 2016). In 2016, Australia identified a penicillin-resistant clade of MenW ST-11 CC isolates belonging to the Original UK strain (Mowlaboccus et al., 2017).

Among the serogroup W ST-11 CC English isolates, six distinct penicillin resistance-associated sublineages (1-6) were identified. Penicillin resistance-associated lineage 1, which contained 16 English PenR isolates, was an expansion of the strain identified in Australia in 2016. Further analysis to include PubMLST isolates identified other serogroup W ST-11 CC isolates from nine countries across Europe and isolates from Canada, Japan and New Zealand, resulting in a total of 122 isolates within penicillin resistance-associated sublineage one. This signifies that this lineage is highly successful in causing IMD due to being widespread and suggests that it is likely to continue causing IMD.

Penicillin resistance-associated lineage 2 included three English PenR isolates from 2017-2019 which harboured *penA14* (five AASs associated with conferring reduced susceptibility and resistance to penicillin). An isolate from Scotland (2019) and an isolate from Sweden (2018) also belonged to penicillin resistance-associated lineage 2 and harbouring *penA14*. *PenA14* has been previously reported among several meningococci with reduced susceptibility to penicillin (Taha et al., 2007). Penicillin resistance-associated lineage 3 included two PenR English isolates from 2018 and 2019 which harboured *penA540* (five AASs associated with penicillin resistance). Given that the strain identified in Australia has spread over the last few years, penicillin resistance-associated lineages 2 and 3 require continued surveillance to monitor the potential spread. Penicillin resistance-associated lineages 4-6, contained just one PenR isolate (*penA* allele 9 or 435; five AASs associated with penicillin resistance), which suggests a transient recombinant that may not be encountered again. Most isolates in these sublineages were identified after 2016 and appear more predominant with time, suggesting that PenR MenW ST-11 CC isolates may continue to rise.

Historically, penicillin has been the antibiotic of choice in the treatment of IMD (Oppenheim, 1997; Sáez-Llorens and McCracken, 1999; van de Beek et al., 2002). Following initial observations of meningococci with reduced susceptibility to penicillin, usual doses of the antibiotic were thought to be effective against such strains (Uriz et al., 1991). However, reports of treatment failure in cases of IMD caused by strains with reduced susceptibility and resistance to penicillin were also reported (Turner et al., 1990; Bardi et al., 1994), which led to the recommendation of higher doses of penicillin (Jones and Sutcliffe, 1990). However, due to the ease of use of 3GCs, combined with inconsistent antibiotic susceptibility testing and increasing penicillin resistance among meningococci, 3GCs have been the preferred first line treatment of IMD over more recent years (Public Health England, 2012; Blain et al., 2016).

In the UK, penicillin is only administered to patients in primary care with suspected IMD prior to the administration of 3GCs in secondary care (National Institute for Health and Care Excellence, 2015). In the USA, whilst either 3GCs or penicillin are recommended for treatment, recent studies suggest that penicillin is rarely used to treat IMD exclusively (Blain et al., 2016). Additionally, following a recent increase in penicillin resistant serogroup

Y meningococci in the USA, is it recommended that penicillin susceptibility of isolates is determined prior to use of the antibiotic in the treatment of IMD (Centers for Diseases Control and Prevention, 2019).

Whilst the relatively limited use of penicillin suggests that the increase in penicillin resistance among meningococci observed in this study may not be as clinically significant as if penicillin was exclusively used in IMD treatment, surveillance and awareness of such resistance remains of importance, particularly for clinicians managing patients at high risk for IMD development, for which penicillin prophylaxis is recommended for IMD prevention.

Individuals with terminal complement deficiencies and those undergoing Eculizumab treatment are at risk for IMD development due to their inability to mediate meningococcal cell lysis by the formation of the MAC (Ladhani et al., 2019). This remains the case even after receipt of preventative meningococcal vaccinations, where effectiveness is unclear in such individuals, with cases of vaccine failures reported (McNamara et al., 2017; Ladhani et al., 2019). Penicillin prophylaxis to further reduce the risk of IMD development is therefore also recommended, however cases of IMD among immunocompromised individuals due to meningococcal strains resistant to or displaying reduced susceptibility to penicillin have been reported (McNamara et al., 2017; Parikh et al., 2017). Awareness and vigilance of strains associated with penicillin resistance, such as the expanding serogroup W ST-11 CC strain identified in this study, is therefore essential for maintaining effective prophylactic regimes and in preventing IMD among high-risk patients.

Even in immunocompetent individuals, not all meningococcal strains are covered by the preventative vaccines. Whilst IMD following vaccination with the ACWY vaccine is rare, the MenB Bexsero vaccine is estimated to cover only 73-88% of meningococcal group B strains (Parikh et al., 2016). Whilst global vaccination is key in the prevention of IMD, antibiotic treatment of the disease and therefore surveillance of antibiotic resistance amongst this species remains paramount.

Most of the PenR isolates identified in this study harboured *penA* alleles that contained the five AASs (F504L, A510V, I515V, H541N, and I566V) associated with penicillin resistance which have been observed among isolates worldwide (Antignac et al., 2003; Vázquez et al., 2003; Taha et al., 2006a; Vacca et al., 2018).

Three PenR isolates possessed *penA* alleles with only a partial set of the AASs associated with conferring reduced susceptibility and resistance to penicillin. One of these harboured *penA327*, which contains four out of the five AASs Penicillin-resistant meningococcal isolates possessing *penA327* has been reported previously (Deghmane et al., 2017). *PenA327* contains an additional AAS; G545S. Forty-one *penA* alleles were identified on PubMLST that contained G545S, three of which did not have any of the five AASs associated with penicillin resistance. MIC data were unavailable for the isolates containing G545S independently of the five AASs. Further work is therefore required to determine the possible role of residue G545, and the absence of I566V, in relation to penicillin resistance. *PenA327* has also been associated with reduced susceptibility to 3GCs (Deghmane et al., 2017). All IMD isolates with *penA327* that were received at the MRU, also displayed reduced susceptibility to cefotaxime (section 4.3).

One PenR isolate received at the MRU harboured *penA209*, an allele that had only three of the AASs associated with conferring reduced susceptibility and resistance to penicillin (F504L, A510V and I515V). The allele also had AASs V447L and A516G. Other *penA* alleles on PubMLST that contained the same three AASs without V447L and A516 had lower penicillin MICs (0.047-0.094 mg/L) compared to those that did have V447L and A516 (0.12-0.5 mg/L). This suggests that *penA* alleles harbouring only these three AASs associated with conferring reduced susceptibility and resistance to penicillin may not be adequate to confer penicillin resistance alone, however, it may be the case that they can cause reduced susceptibly and resistance to penicillin when in combination with V447 and A516. Future work is therefore needed to confirm the role that these AASs have in conferring resistance to penicillin. *PenA* alleles containing V447 and A516 were found among a much larger proportion of gonococcal isolates on PubMLST compared to meningococcal isolates, which suggest that these AASs may have originated in this species and were introduced into meningococci during a HGT event.

One PenR isolate (MIC = 0.38 mg/L, serogroup W ST-11 CC) harboured *penA171,* an allele which contained none of the AASs associated with conferring reduced susceptibility and resistance to penicillin. *PenA171* contained AAS P551S, which has been observed among gonococcal isolates resistant to penicillin (Whiley et al., 2010). However, this study did not confirm whether the *penA* alleles harboured by these gonococcal isolates also contained

the five AASs associated with penicillin resistance among meningococcal isolates. Other meningococcal isolates that possessed *penA171* were identified on the PubMLST database and were penicillin-susceptible, signifying that *penA171,* and the P551S AAS alone, are not responsible for causing penicillin resistance among meningococci. This suggests that another mechanism may be responsible for causing penicillin resistance in this PenR isolate and further work is therefore required to determine the cause. Penicillin resistance among meningococci caused by the production of beta-lactamase is rare and is associated with isolates displaying higher levels of penicillin resistance (MICs >2 mg/L) (Dillon et al., 1983; Botha, 1988; Fontanals et al., 1989). This isolate was beta-lactamase negative, which reflects the relatively low level of penicillin resistance displayed (MIC = 0.38 mg/L). Alternative mechanisms of penicillin resistance have been determined among *N. gonorrhoeae*, which include mutations in the transcriptional repressor of the efflux pump (mtrCDE) operon, which is encoded by the *mtrR* gene (Maness and Sparling, 1973). The operation of the mtrCDE efflux pump in meningococci appears to differ than in that of *N. gonorrhoeae* (Rouquette-Loughlin et al., 2004), where the mtrCDE operon is not subject to the *mtrR* regulatory scheme, and there is no evidence to suggest that mutations in the *mtrR* gene of meningococci can cause penicillin resistance as in gonococci.

4.2 Ciprofloxacin susceptibility among IMD isolates in England, Wales and Northern Ireland

Out of the 4,122 IMD isolates received at the MRU from July 2010 to June 2019, five were ciprofloxacin-resistant).

Each of the ciprofloxacin-resistant isolates harboured AASs in the *gyrA* gene (D95N or T91I) which have previously been associated with conferring ciprofloxacin resistance among meningococcal isolates worldwide (Skoczyńska et al., 2008; Hong et al., 2013; Tsang et al., 2017). The ciprofloxacin-resistant isolate with the highest MIC (MIC = 0.5 mg/L) also harboured an AAS in its *parC* allele (D86N). Mutations in *parC* among meningococcal isolates which also harbour mutations in *gyrA* have been shown to cause enhanced levels of resistance to ciprofloxacin (MICs of 0.5–1 mg/L). This is therefore likely to have caused the high level of ciprofloxacin resistance observed in this isolate.

The five ciprofloxacin-resistant isolates received at the MRU belonged to five different clonal complexes. In China, where ciprofloxacin resistance is prevalent, resistance is commonly seen among isolates belonging to ST-4821 CC, which has also been observed among ciprofloxacin-resistant isolates in other countries (Zhu et al., 2014; Tsang et al., 2017; Kawasaki et al., 2018). In the USA, a recent study identified ciprofloxacin resistance among several meningococcal isolates belonging to ST-23 CC (McNamara et al., 2020). These also produced beta-lactamase rendering them resistant to penicillin. Since the ciprofloxacin-resistant isolates in the present study do not seem to be prevalent among a certain clonal complex, it may suggest that these particular meningococcal strains have not successfully expanded with the altered *gyrA* alleles and suggests that levels of ciprofloxacin resistance may continue to remain low within the population. Further work may be performed to determine whether the mutations responsible for ciprofloxacin in these isolates were due to single nucleotide polymorphisms or arose through recombination. This may be achieved by performing phylogenetic analyses with available CC-matched genomes to find closest relatives followed by pairwise alignments of *gyrA* with these.

In July 2019, after the study period for ABR among IMD isolates in E, W and NI 2010/11-2018/19, three NG ciprofloxacin-resistant (meningococcal isolates were received at the MRU. The isolates were invasive (n=1) and conjunctivitis (n=2) case isolates from England, and were characterised as belonging to ST-175 CC.

A phylogenetic analysis of all available ST-175 CC genomes within the PubMLST database identified a sublineage of NG ST-175 CC isolates, which included the genomes of the three English isolates and genomes of eight other isolates responsible for causing IMD across Europe since 2015. Seven out of these 11 isolates were ciprofloxacin-resistant and harboured altered *gyrA* alleles (*gyrA187* and *gyrA313*) with AAS T91I. The *gyrA* alleles were found to be of *Neisseria cinerea* origin, highlighting the important role of HGT in the spread of ABR genes among the *Neisseria* species (Chen et al., 2020). Given that bacteria that are closely related have a higher propensity for HGT (Didelot and Maiden, 2010), the fact that these *gyrA* alleles of *N. cinerea* origin have been able to establish a steady existence in the ST-175 CC is concerning, as they may go on to establish a presence within more virulent encapsulated strains of meningococci.

Another sublineage of the ST-175 CC contained carriage isolates (n=4) that all harboured a different altered *gyrA* allele (*gyrA152*) with AAS D95N, whilst the isolates comprising the other ST-175 CC sublineages did not harbour altered *gyrA* alleles.

The three English NG cases were linked to recent travel to Mecca, KSA (Public Health England, 2019). Three other NG ST-175 CC IMD isolates, isolated in Germany, were from asylum seekers originally from Afghanistan and Nigeria. Asylum seekers may experience crowded conditions which has been associated with the spread of meningococcal carriage (Brundage et al., 2002; Tully et al., 2006; Yezli, 2018). This suggests that the NG ST-175 CC strain could be more widely distributed, and that further unreported cases may have occurred. This highlights the necessity of worldwide genomic surveillance of IMD and ABR, and the Global Meningitis Genome Partnership (Rodgers et al., 2020) has been created to enable all nations to do so as part of the 'Global Roadmap to Defeat Meningitis by 2030' (World Health Organization, 2020).

Outbreaks of meningococcal disease have previously been associated with pilgrimages to Mecca, KSA (Moore et al., 1989; Al-Gahtani et al., 1995; Aguilera et al., 2002). Consequently, since 2002, all pilgrims have been required to be vaccinated with the MenACWY polysaccharide vaccine prior to travelling, which has since prevented any further outbreaks (Yezli, Bin Saeed, et al., 2016). This vaccine, however, does not prevent IMD caused by NG meningococci and, thus, this NG ST-175 CC strain. It would also not prevent carriage acquisition (Wilder-Smith et al., 2003b; Nicolas et al., 2005; Ceyhan et al., 2013). In addition, prophylaxis with ciprofloxacin is compulsory for travellers to KSA from countries of the African meningitis belt. This would not be effective against ciprofloxacin-resistant strains including this NG ST-175 CC strain. Millions of doses of ciprofloxacin are thought to have been distributed to pilgrims over the last ten years (Zumla and Memish, 2019), and, with the emergence of meningococcal ciprofloxacin resistance, the benefits of ciprofloxacin prophylaxis among travellers to KSA have been challenged (Memish et al., 2017).

NG meningococci are seldom responsible for IMD among healthy individuals, with NG disease mainly reported among immunocompromised individuals with terminal complement deficiencies (Ladhani et al., 2019). Among the nine NG ST-175 CC IMD isolates, five were isolated from individuals with immune deficiencies. Immunocompromised

individuals are usually recommended to have preventative meningococcal vaccinations; MenACWY conjugate and MenB subcapsular vaccines. MenB vaccines can offer protection from other strains irrespective of serogroup, including NG strains, but is dependent upon sufficient expression and cross reactivity of one of the sub-capsular vaccine antigens (Jiang et al., 2010; Serruto et al., 2012). Vaccine effectiveness among individuals with complement system deficiencies is uncertain, however, with cases of IMD still reported despite receipt of preventative meningococcal vaccinations (McNamara et al., 2017).

Some countries, such as the UK and France, also recommend chemoprophylaxis with antibiotics for immunocompromised individuals, in addition to the recommended preventative vaccinations (Nolfi-Donegan et al., 2018). Penicillin is usually the chemoprophylactic agent of choice, however penicillin-resistant IMD strains have been known to subvert such regimes (McNamara et al., 2017; Parikh et al., 2017). All nine NG ST-175 CC IMD isolates displayed reduced susceptibility or resistance to penicillin (MICs = 0.094–0.5 mg/L). Although the penicillin MICs were mostly relatively low, one isolate did have an MIC of 0.5 mg/L. This level of penicillin resistance was observed in an isolate causing IMD in an immunocompromised patient receiving penicillin prophylaxis (Parikh et al., 2017). This NG ST-175 CC strain is therefore particularly concerning for immunocompromised individuals, and low-level penicillin prophylaxis doses may be ineffective.

Occasionally, ciprofloxacin may be recommended to immunocompromised individuals or prescribed as a rescue therapy for when symptoms of IMD occur despite other prophylactic regimes (Nester et al., 2011; Noone et al., 2012; Struijk et al., 2013; Hawkins et al., 2017). In the UK, ciprofloxacin is also the first-choice antibiotic for chemoprophylaxis of close contacts of patients with IMD. Ciprofloxacin will be ineffective against this NG ST-175 CC ciprofloxacin-resistant strain, thus highlighting the continued need for surveillance of ABR amongst IMD isolates. It also highlights the need for vigilance in the use of ciprofloxacin for those close contacts of patients presenting with IMD on return from travel.

4.3 Cefotaxime susceptibility among IMD isolates (2010/11-2018/19)

Out of the 4,122 IMD isolates received at the MRU from July 2010 to June 2019, only seven had cefotaxime MICs ≥ 0.047 mg/L, and therefore isolates with these elevated cefotaxime MICs were rare. One of the isolates was cefotaxime-resistant (MIC = 0.25 mg/L).

One of the isolates (MIC = 0.047 mg/L, *penA11*) was serogroup B and had an incomplete MLST profile with an exact match for ST-1867 for five loci. The isolate did not possess fHbp or NadA; important antigens for the MenB vaccines. Several meningococcal isolates belonging to ST-1867 CC have previously been identified which lack fHbp (Lucidarme et al., 2011). Whilst such strains are rare, given a possible association of sub-capsular vaccine subversion with decreasing antibiotic susceptibility, surveillance of these and their associated ABR is essential to monitor their potential expansion.

Five of the seven isolates harboured *penA327* (MICs = 0.047–0.125 mg/L), four of which were serogroup C belonging to ST-11 CC and one which was serogroup B belonging to ST-41/44 CC. *PenA327* has already been identified among meningococcal isolates associated with reduced susceptibility to both cefotaxime and penicillin. A study by Deghmane and colleagues identified 25 meningococcal isolates harbouring *penA327* which all belonged to ST-11 CC of serogroups B and C, suggesting successful clonal expansion of this particular strain potentially involving capsular switching (Deghmane et al., 2017). As further work, the distribution of this allele on a cgMLST phylogeny of ST-11 CC may be performed to see how widespread the gene is and whether it affects one or more sublineages.

PenA327 is identical to that of an allele (penAXXXIV) identified among gonococcal isolates displaying resistance to ceftriaxone in this species (Ohnishi et al., 2011). *PenA327* has previously been identified among several isolates causing IMD in men who have sex with men and has also been identified in isolates from meningococcal urethritis cases (Taha et al., 2016; Deghmane et al., 2017). As gonococci infect the urogenital tract, the identification of *penA327* among isolates from meningococci urethritis cases, suggests acquisition of the allele during a HGT event during mixed gonococcal urethritis infection. Increasing numbers of urogenital and rectal meningococcal infections have been reported over recent years, including those identifying the co-colonisation of hyperinvasive penicillin-resistant meningococcal strains and multi-drug resistant gonococci (Odile B Harrison et al., 2017).

Over the past few years, the emergence of a NG meningococcal strain associated with meningococcal urethritis has been identified across the USA (Bazan et al., 2017; Retchless et al., 2018). This strain appears to have acquired genes from *N. gonorrhoeae* that allow capability of nitrate dependant anaerobic growth (Tzeng et al., 2017). NG (unencapsulated) meningococci rarely cause invasive disease due to lack of capsule protection from complement mediated killing, however invasive cases caused by this NG clade have been reported, although it was not known whether cases were among immunocompetent individuals (Retchless et al., 2018). Although acquisition of ABR genes amongst this NG clade has not been reported, the acquisition of other gonococcal genes among meningococci, including *penA327*, in combination with the increasing identification of co-colonisation of both species, is a cause for concern. It suggests that meningococci may continue to acquire gonococcal genes in the future, which could result in increasing numbers of antibiotic resistant meningococci with a potential to threaten the future treatment and prevention of IMD.

Apart from *penA327*, no other *penA* allele has yet been associated with reduced susceptibility or resistance to 3GCs among meningococci. *PenA327* is similar to a gonococcal *penA* allele (penA-C1) which has the AAS A501P and has been associated with high levels of 3GC resistance among gonococcal isolates (Unemo et al., 2012). Other AASs at this position, A501T and A501V have also been described among gonococcal isolates displaying reduced susceptibility to cefotaxime (Whiley et al., 2007; Tomberg et al., 2017). Amino acid 501 is positioned close to the core of the active site motif of PBP2 (Tomberg et al., 2010). It is thought that the substitution of methyl side chain alanine (A501) with larger side chains threonine (A501T) and valine (A501V) prevents effective binding of 3GCs, and proline substitutions (A501P) result in further structural modifications causing higher levels of 3GC resistance (Unemo et al., 2012).

The cefotaxime-resistant meningococcal isolate identified in this study harboured *penA419*. There were two AASs in the *penA* allele harboured by the cefotaxime-resistant isolate that were unique when compared to cefotaxime-susceptible penicillin-resistant isolates; A501T, previously seen among gonococci with reduced susceptibility to cefotaxime and D511V. Other isolates with *penA* alleles with AASs at positions 501 and 511 were identified on PubMLST and further isolates stored at the MRU (non-MGL) with

elevated cefotaxime MICs were also identified. Another unique AAS was identified among the non-MGL isolates that was harboured by isolates with reduced susceptibility to cefotaxime; N572D.

MICs of isolates harbouring *penA* alleles with A501V were 0.003–0.012 mg/L while those with A501T were 0.047-0.125 mg/L. *PenA* alleles with AASs at D511 (D511V or D511G) in addition to A501T were 0.125-0.25 mg/L. MICs of isolates harbouring alleles with N572D were 0.047-0.125 mg/L. This suggests that AAS A501V does not confer reduced susceptibility to cefotaxime in meningococci, unlike in gonococci (Tomberg et al., 2017), whilst A501T may. When A501T was present in combination with an AAS at 511 (D511V or D511G), cefotaxime MICs among the meningococcal isolates were enhanced.

PenA alleles with AASs at D511 are extremely rare, with only five *penA* alleles identified on PubMLST and six corresponding isolates. Further work is therefore required to determine the role that these AASs play in susceptibility to cefotaxime among meningococci. A501P, an AAS present in *penA* alleles among gonococcal isolates with reduced susceptibility to 3GC, was not identified among any meningococcal *penA* alleles in this study. However, it has been suggested that this mutation may eventually be selected in meningococci (Zapun et al., 2016), especially given that *penA327* was likely acquired by gonococci through HGT during co-colonisation. Whilst resistance to 3GC remains extremely rare among meningococci continued surveillance of resistance and reduced susceptibility to 3GCs is vital to ensure continued effective use in the treatment of IMD.

Ceftriaxone is currently the final remaining treatment option for *N. gonorrhoeae* in many countries, for which treatment failures are still identified (Unemo, 2015). Failure to develop new effective antibiotics for the ever-increasing numbers of gonococcal infections could eventually contribute to increasing ABR among meningococci in the future, given the use of similar antibiotics and increasing reports of co-colonisation and opportunities for HGT between the two species. Major efforts in vaccine development for *N. gonorrhoeae* in recent years have, however, identified new targets in the hope to combat ABR gonococci (Lin et al., 2021).

In gonococci, mutations in the *mtrR* gene have previously been associated with reduced susceptibility to 3GCs (Lindberg et al., 2007; Zhao et al., 2009). The *mtrR* allele possessed by the cefotaxime-resistant IMD isolate in the present study was *mtrR249.* There was a frameshift at the beginning of the gene (AA position 5), however there were no other isolates on PubMLST harbouring this or other *mtrR* genes with a frameshift at a similarly early position. Those with frameshifts later in the gene were cefotaxime-susceptible. It might be speculated that the corresponding, relatively less-truncated, products are still able to function, however, it has been suggested that mtrCDE efflux pump is independent of the *mtrR* gene among meningococci (Rouquette-Loughlin et al., 2004), and with no studies suggesting mutations in the *mtrR* gene causes ABR among this species, it is unlikely that the *mtrR* gene is responsible for the cefotaxime resistance displayed by this isolate. Further research is required to determine the role that the *mtrR* gene may play in ABR among meningococci.

4.4 Rifampicin susceptibility among IMD isolates (2010/11-2018/19)

Out of the 4,122 IMD isolates received at the MRU from 2010/11-2018/19, only two were resistant to rifampicin.

Whilst resistance to rifampicin has been reported among meningococci, it is rare given its widespread use as a prophylactic agent. The majority of meningococcal rifampicin resistance is found among isolates from cases of close contacts following rifampicin prophylaxis (Rainbow et al., 2005; M. Taha et al., 2006b). However, rifampicin resistance has also been observed among index cases (Stefanelli et al., 2001; Skoczynska et al., 2009). There was no evidence to suggest that the two rifampicin-resistant isolates received at the MRU were from close contact cases.

One rifampicin-resistant isolate (MIC = 0.5 mg/L) was serogroup C belonging to ST-11 CC harbouring *rpoB238*, whilst the other rifampicin-resistant isolate (MIC = >32 mg/L) was serogroup B belonging to ST-41/44 CC harbouring *rpoB84*. When aligned to a WT *rpoB* allele (allele 1), *rpoB238* harboured one AAS (D545E) whilst *rpoB84* harboured four (H555N, I624V, D625N, S654K). Amino acid substitutions at AA positions 545 and 555 have been

reported among rifampicin-resistant meningococcal isolates, with mutations at AA position 555 associated with higher levels of resistance than those with mutations at AA position 545 (Taha et al., 2010). Previous studies have also identified the same AASs among multiple isolates with varying levels of rifampicin resistance (Carter et al., 1994; Stefanelli et al., 2001). This, along with the observed difference in rifampicin MIC values displayed by the two resistant isolates in this study, may indicate that additional unknown mechanisms can cause increased levels of resistance among meningococci, and further work is needed to identify such factors.

Mutations in the *mtrR* gene have been associated with increased levels of rifampicin resistance among gonococcal isolates (Hagman et al., 1995; Rouquette-Loughlin et al., 2004). However, the *mtrR* alleles possessed by the two rifampicin-resistant isolates in this study were also observed among rifampicin-susceptible isolates in this study, suggesting that this gene did not contribute to the observed rifampicin resistance.

Rifampicin resistance has been observed among meningococcal isolates from a range of CCs (Stefanelli et al., 2001; M. Taha et al., 2006b). Resistance to rifampicin was rare among meningococcal isolates in this study and observed among different clonal complexes, suggesting a lack of clonal expansion. It has been suggested that mutations in the *rpoB* gene causes a biological fitness cost to meningococci, and a lack of survival in the bloodstream has been demonstrated in mice models (Colicchio et al., 2015).

Despite the low levels of rifampicin resistance observed among IMD isolates in this study, continued monitoring of ABR among meningococci is essential to ensure that the low levels of rifampicin resistance remain. This will ensure the continued effective use of rifampicin as a chemoprophylactic agent, which may be administered as a suitable alternative to ciprofloxacin, for example against ciprofloxacin-resistant strains.

4.5 Conclusion and further work

From 2010/11-2018/19, ABR was rare among IMD isolates from E, W and NI. However, resistance to all four antibiotics (penicillin, rifampicin, cefotaxime and ciprofloxacin) was

observed among the IMD isolates. Only one isolate was resistant to more than one antibiotic (penicillin and cefotaxime).

Out of the four antibiotics, meningococcal resistance to penicillin was the most common and appeared to become more prevalent over the last four years (2015/16 – 2018/19), with the highest annual proportion of penicillin-resistant isolates (MICs > 0.38 mg/L) observed in the final year of the study period (2018/19), where 7% of IMD isolates were penicillin-resistant. The proportion of IMD isolates displaying reduced susceptibility to penicillin (MICs = 0.094-0.25 mg/L) remained fairly consistent each year, representing 34% of IMD isolates over the whole study period, however was highest in the final year of the study period, where 41% of IMD isolates displayed reduced susceptibility to penicillin.

Penicillin resistance among the IMD isolates was mainly due to altered *penA* genes containing all five of the AASs previously associated with conferring penicillin resistance among meningococci. Penicillin resistance was also observed among IMD isolates possessing *penA* genes with only four of these AASs; *penA* allele 327, which has also been shown to be responsible for conferring penicillin resistance among meningococci. One penicillin-resistant IMD isolate harboured a *penA* gene with only three of these AASs (*penA209*), an allele which possessed additional AASs (V447L and A516G) and which were associated with meningococcal isolates displaying higher penicillin MIC values compared to *penA* alleles with only the three AASs without the additional AASs. One penicillin-resistant IMD isolate harboured a *penA* gene with none of the five AASs. The isolate harboured an *mtrR* allele (*mtrR217*) which was unique to this isolate on PubMLST. However, the *mtrR* allele possessed an AAS (S32W) found among other *mtrR* alleles among gonococcal isolates on PubMLST that were penicillin-resistant and whose *penA* alleles did not contain all five of the AASs previously associated with conferring resistance to penicillin. Further work is needed to determine whether this *mtrR* gene, or any of the other unique genes identified in this isolate, can cause penicillin resistance among meningococci.

Over the last four years (2015/16-2018/19) an annual increase in the proportion of penicillin-resistant serogroup W IMD isolates belonging to CC11 was observed. This coincides with the time in which Australia reported the emergence of a penicillin-resistant clade of serogroup W ST-11 CC isolates. Phylogenetic analysis of serogroup W ST-11 CC isolates from England and the rest of the world identified an expansion of the penicillin-

resistant Australian clade to include several penicillin-resistant serogroup W ST-11 CC isolates harbouring *penA9* from England and several other countries from across the globe. A second expanding penicillin resistant-associated lineage of serogroup W ST-11 CC isolates harbouring *penA14* from England and European countries was also identified.

Isolates in these lineages were more frequently identified after 2016, becoming more prevalent with time, indicating successful clonal expansion and suggesting that the number of penicillin-resistant serogroup W ST-11 CC isolates may continue to increase over the coming years. Surveillance of penicillin resistance among IMD isolates with close monitoring of serogroup W ST-11 CC isolates is therefore paramount to ensure successful use of the antibiotic in treatment and as a chemoprophylactic agent.

Five ciprofloxacin-resistant IMD isolates identified from 2010/11-2018/19 all belonged to different clonal complexes and all harboured different *gyrA* alleles, each with AASs associated with conferring ciprofloxacin resistance among meningococci. However, following an outbreak of meningococcal disease in England in July 2019, one strain of meningococci that was responsible for causing several cases of meningococcal disease throughout Europe, belonging to ST-175 CC, was identified.

The strain comprised NG isolates and is therefore especially virulent among individuals with complement deficiencies who are at higher risk of IMD development and where vaccine effectiveness is unknown. As well as immunocompromised individuals, the ciprofloxacin-resistant NG ST-175 CC isolates were also found among pilgrims and asylum seekers, suggesting that strain may be circulating worldwide and with potentially more cases that may have gone unreported. Clinicians should continue to be vigilant when such individuals present with meningococcal disease to ensure effective treatment and prophylaxis regimes are maintained.

Several IMD isolates from 2010/11-2018/19 that were penicillin-resistant also displayed reduced susceptibility to cefotaxime (cefotaxime MICs ≥ 0.047 mg/L). Most of these isolates harboured *penA327*, an allele already proven to cause reduced susceptibility to 3GCs among meningococci. One isolate that displayed both penicillin and cefotaxime resistance harboured *penA419*, which, in addition to the five AASs associated with conferring penicillin resistance among meningococci, had other unique AASs: A501T and

D511A. A wider search on PubMLST identified further isolates with *penA* alleles with AASs at these AA positions. Isolates with AASs at D511 were rare, with only five additional isolates identified. Where MIC values were available, the isolates displayed reduced susceptibility to cefotaxime (0.125 mg/L). Isolates with *penA* alleles with the AAS A501T alone also displayed reduced susceptibility to cefotaxime but MIC values were much lower than in isolates that harboured *penA* alleles with AASs at both AA positions.

Further work is needed to confirm the role that these AASs have in conferring reduced susceptibility and resistance to cefotaxime.

This study identified several IMD isolates with resistance to antibiotics used for current treatment and prophylaxis of IMD. It also identified emerging threats and the progression of antibiotic resistance among strains over time. Sustained surveillance of ABR among the meningococcal population is therefore vital to maintain successful treatment regimens for IMD and chemoprophylaxis regimes, in particular for those already at a greater risk of IMD development.

5 References

Abad, R., Lopez, E. L., Debbag, R. and Vázquez, J. A. (2014) 'Serogroup W meningococcal disease: global spread and current affect on the Southern Cone in Latin America.' *Epidemiology and Infection*. 2014/05/15, Cambridge University Press, 142(12) pp. 2461–2470.

Abadi, F. J. R., Carter, P. E., Cash, P. and Pennington, T. H. (1996) 'Rifampin resistance in *Neisseria meningitidis* due to alterations in membrane permeability.' *Antimicrobial Agents and Chemotherapy*, 40(3) pp. 646–651.

Abraham, E.P and Chain, E. (1940) 'An enzyme from bacteria able to destroy penicillin.' *Reviews of Infectious Diseases*, 10(4) pp. 677–678.

Aguilera, J. F., Perrocheau, A., Meffre, C. and Hahné, S. (2002) 'Outbreak of serogroup W135 meningococcal disease after the Hajj pilgrimage, Europe, 2000.' *Emerging Infectious Diseases*, 8(8) pp. 761–767.

Al-Gahtani, Y. M., El Bushra, H. E., Al-Qarawi, S. M., Al-Zubaidi, A. A. and Fontaine, R. E. (1995) 'Epidemiological investigation of an outbreak of meningococcal meningitis in Makkah (Mecca), Saudi Arabia, 1992.' *Epidemiology and Infection*. Cambridge University Press, 115(3) pp. 399–409.

Alcalá, B., Salcedo, C., de la Fuente, L., Arreaza, L., Uría, M. J., Abad, R., Enríquez, R., Vázquez, J. A., Motgé, M. and de Batlle, J. (2004) '*Neisseria meningitidis* showing decreased susceptibility to ciprofloxacin: first report in Spain.' *Journal of Antimicrobial Chemotherapy*, 53(2) p. 409.

Alfsnes, K., Frye, S. A., Eriksson, J., Eldholm, V., Brynildsrud, O. B., Bohlin, J., Harrison, O. B., Hood, D. W., Maiden, M. C. J., Tønjum, T. and Ambur, O. H. (2018) 'A genomic view of experimental intraspecies and interspecies transformation of a rifampicin-resistance allele into *Neisseria meningitidis*.' *Microbial Genomics*. Microbiology Society, 4(11) pp. 2–14.

Almog, R., Block, C., Gdalevich, M., Lev, B., Wiener, M. and Ashkenazi, S. (1994) 'First

recorded outbreaks of meningococcal disease in the Israel Defence Force: three clusters due to serogroup C and the emergence of resistance to rifampicin.' *Infection*. Germany, 22(2) pp. 69–71.

Ambur, O. H., Frye, S. A. and Tønjum, T. (2007) 'New functional identity for the DNA uptake sequence in transformation and its presence in transcriptional terminators.' *Journal of Bacteriology*, 189(5) pp. 2077–2085.

Andrews, J. M. (2001) 'Determination of minimum inhibitory concentrations.' *The Journal of antimicrobial chemotherapy*. England, 48 Suppl 1, July, pp. 5–16.

Antignac, A., Boneca, I. G., Rousselle, J.-C., Namane, A., Carlier, J.-P., Vázquez, J. A., Fox, A., Alonso, J.-M. and Taha, M.-K. (2003) 'Correlation between alterations of the penicillin-binding protein 2 and modifications of the peptidoglycan structure in *Neisseria meningitidis* with reduced susceptibility to penicillin G.' *The Journal of biological chemistry*. American Society for Biochemistry and Molecular Biology, 278(34) pp. 31529–35.

Araya, P., Fernández, J., Del Canto, F., Seoane, M., Ibarz-Pavón, A. B., Barra, G., Pidal, P., Díaz, J., Hormazábal, J. C. and Valenzuela, M. T. (2015) '*Neisseria meningitidis* ST-11 clonal complex, Chile, 2012.' *Emerging Infectious Diseases*, 21(2) pp. 339–341.

Arnold, L., Borrow, R., Riley, K., Munir, T., Kelly, R., Jones, R., Gachev, J., Forrest, B., Pike, A., Muus, P., Hillmen, P. and Griffin, M. (2020) 'Management of meningococcal disease risk in patients with Paroxysmal Nocturnal Hemoglobinuria (PNH) on complement inhibitors: 18 years' experience from the UK National PNH Service in Leeds.' *Blood*, 136(Supplement 1) pp. 5–6.

Arnold, R., Galloway, Y., McNicholas, A. and O'Hallahan, J. (2011) 'Effectiveness of a vaccination programme for an epidemic of meningococcal B in New Zealand.' *Vaccine*. Netherlands, 29(40) pp. 7100–7106.

Bäckman, A., Orvelid, P., Vazquez, J. A., Sköld, O. and Olcén, P. (2000) 'Complete sequence of a β-lactamase-encoding plasmid in *Neisseria meningitidis*.' *Antimicrobial Agents and Chemotherapy*, 44(1) pp. 210–212.

Balmer, P., Borrow, R. and Miller, E. (2002) 'Impact of meningococcal C conjugate vaccine

in the UK.' *Journal of Medical Microbiology*, 51(9) pp. 717–722.

Baraldo, K., Mori, E., Bartoloni, A., Norelli, F., Grandi, G., Rappuoli, R., Finco, O. and Giudice, G. Del (2005) 'Combined conjugate vaccines : enhanced immunogenicity with the N19 polyepitope as a carrier protein,' 73(9) pp. 5835–5841.

Bardi, L., Badolati, A., Corso, A. and Rossi, M. A. (1994) 'Failure of the treatment with penicillin in a case of *Neisseria meningitidis* meningitis.' *Medicina*. Argentina, 54 pp. 427–430.

Baxter, R., Keshavan, P., Welsch, J. A., Han, L. and Smolenov, I. (2016) 'Persistence of the immune response after MenACWY-CRM vaccination and response to a booster dose, in adolescents, children and infants.' *Human Vaccines and Immunotherapeutics*. Taylor and Francis Inc. pp. 1300–1310.

Bazan, J. A., Turner, A. N., Kirkcaldy, R. D., Retchless, A. C., Kretz, C. B., Briere, E., Tzeng, Y.-L., Stephens, D. S., Maierhofer, C., Del Rio, C., Abrams, A. J., Trees, D. L., Ervin, M., Licon, D. B., Fields, K. S., Roberts, M. W., Dennison, A. and Wang, X. (2017) 'Large cluster of *Neisseria meningitidis* urethritis in Columbus, Ohio, 2015.' *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, 65(1) pp. 92–99.

van de Beek, D., de Gans, J., Spanjaard, L., Vermeulen, M. and Dankert, J. (2002) 'Antibiotic guidelines and antibiotic use in adult bacterial meningitis in The Netherlands.' *Journal of Antimicrobial Chemotherapy*, 49(4) pp. 661–666.

Berkey, P., Rolston, K., Zukiwski, A., Gooch, G. and Bodey, G. P. (1988) 'Rifampin-resistant meningococcal infection in a patient given rifampin chemoprophylaxis.' *AJIC: American Journal of Infection Control*, 16(6) pp. 250–252.

Bertrand, S., Carion, F., Wintjens, R., Mathys, V. and Vanhoof, R. (2012) 'Evolutionary changes in antimicrobial resistance of invasive *Neisseria meningitidis* isolates in Belgium from 2000 to 2010: Increasing prevalence of penicillin nonsusceptibility.' *Antimicrobial Agents and Chemotherapy*, 56(5) pp. 2268–2272.

Birtles, A., Hardy, K., Gray, S. J., Handford, S., Kaczmarski, E. B., Edwards-Jones, V. and Fox, A. J. (2005) 'Multilocus sequence typing of *Neisseria meningitidis* directly from clinical samples and application of the method to the investigation of meningococcal

disease case clusters.' *Journal of Clinical Microbiology*, 43(12) pp. 6007–6014.

Bjune, G., Høiby, E. A., Grønnesby, J. K., Arnesen, O., Fredriksen, J. H., Halstensen, A., Holten, E., Lindbak, A. K., Nøkleby, H. and Rosenqvist, E. (1991) 'Effect of outer membrane vesicle vaccine against group B meningococcal disease in Norway.' *Lancet (London, England)*. England, 338(8775) pp. 1093–1096.

Blain, A. E., Mandal, S., Wu, H., MacNeil, J. R., Harrison, L. H., Farley, M. M., Lynfield, R., Miller, L., Nichols, M., Petit, S., Reingold, A., Schaffner, W., Thomas, A., Zansky, S. M., Anderson, R., Harcourt, B. H., Mayer, L. W., Clark, T. A. and Cohn, A. C. (2016) 'Penicillin use in meningococcal disease management: Active bacterial core surveillance sites, 2009.' *Open forum infectious diseases*. Oxford University Press, 3(3) p. 152.

Bond, K. A., Stevens, K., Bulach, D., Carville, K., Ong, K. S. and Howden, B. P. (2016) 'Rising incidence of invasive meningococcal disease caused by *Neisseria meningitidis* serogroup W in Victoria.' *The Medical journal of Australia*, 204(7) pp. 265–266.

Botha, P. (1988) 'Penicillin-resistant *Neisseria meningitidis* in southern Africa.' *Lancet (London, England)*. England p. 54.

Bowler, L. D., Zhang, Q. Y., Riou, J. Y. and Spratt, B. G. (1994) 'Interspecies recombination between the *penA* genes of *Neisseria* meningitidis and commensal *Neisseria* species during the emergence of penicillin resistance in N. meningitidis: Natural events and laboratory simulation.' *Journal of Bacteriology*. American Society for Microbiology, 176(2) pp. 333–337.

Brandtzaeg, P., Kierulf, P., Gaustad, P., Skulberg, A., Bruun, J. N., Halvorsen, S. and Sorensen, E. (1989) 'Plasma endotoxin as a predictor of multiple organ failure and death in systemic meningococcal disease.' *Journal of Infectious Diseases*, 159(2) pp. 195–204.

Bratcher, H. B., Corton, C., Jolley, K. A., Parkhill, J. and Maiden, M. C. J. (2014) 'A gene-by-gene population genomics platform: De novo assembly, annotation and genealogical analysis of 108 representative *Neisseria meningitidis* genomes.' *BMC Genomics*, 15(1) pp. 1–16.

Bratcher, H. B., Rodrigues, C. M. C., Finn, A., Wootton, M., Cameron, J. C., Smith, A., Heath, P., Ladhani, S., Snape, M. D., Pollard, A. J., Cunningham, R., Borrow, R., Trotter, C.,

Gray, S. J., Maiden, M. C. J. and Maclennan, J. M. (2019) 'UKMenCar4: A cross-sectional survey of asymptomatic meningococcal carriage amongst UK adolescents at a period of low invasive meningococcal disease incidence [version 2; peer review: 2 approved].' *Wellcome Open Research*, 4.

Brehony, C., Hill, D. M., Lucidarme, J., Borrow, R. and Maiden, M. C. (2015) 'Meningococcal vaccine antigen diversity in global databases.' *Eurosurveillance*, 20(49) pp. 1–9.

Brehony, C., Jolley, K. A. and Maiden, M. C. J. (2007) 'Multilocus sequence typing for global surveillance of meningococcal disease.' *FEMS Microbiology Reviews*, 31(1) pp. 15–26.

Brouwer, M. C., Tunkel, A. R. and Van De Beek, D. (2010) 'Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis.' *Clinical Microbiology Reviews*, 23(3) pp. 467–492.

Brundage, J. F., Ryan, M. A. K., Feighner, B. H. and Erdtmann, F. J. (2002) 'Meningococcal disease among United States military service members in relation to routine uses of vaccines with different serogroup-specific components, 1964–1998.' *Clinical Infectious Diseases*, 35(11) pp. 1376–1381.

Cai, B., Deitch, E. A. and Ulloa, L. (2010) 'Novel insights for systemic inflammation in sepsis and hemorrhage.' D'Acquisto, F. (ed.) *Mediators of Inflammation*. Hindawi Publishing Corporation, 2010 pp. 1–9.

Campbell, H., Edelstein, M., Andrews, N., Borrow, R., Ramsay, M. and Ladhani, S. (2017) 'Emergency meningococcal ACWY vaccination program for teenagers to control group W meningococcal disease, England, 2015-2016.' *Emerging infectious diseases*. United States, 23(7) pp. 1184–1187.

Capecchi, B., Adu-Bobie, J., Di Marcello, F., Ciucchi, L., Masignani, V., Taddei, A., Rappuoli, R., Pizza, M. and Aricò, B. (2005) '*Neisseria meningitidis* NadA is a new invasin which promotes bacterial adhesion to and penetration into human epithelial cells.' *Molecular Microbiology*, 55(3) pp. 687–698.

Carr, J., Plested, E., Aley, P., Camara, S., MacLennan, J., Gray, S., Borrow, R., Maiden, M. C.

J., Christensen, H., Trotter, C., Finn, A. and Snape, M. (2018) *Be on the TEAM (Teenagers Against Meningitis): a clinical trial evaluating the impact of two licensed group B meningococcal vaccines on pharyngeal carriage of meningococcus in adolescents.* Oral Poster Presentation OP171. 21st International Pathogenic *Neisseria* Conference, California, USA, September 23 – 28. [Online] https://neisseria.org/ipnc/2018/IPNC2018_abstracts.pdf.

Carter, P. E., Abadi, F. J. R., Yakubu, D. E. and Pennington, T. H. (1994) 'Molecular characterization of rifampin-resistant *Neisseria meningitidis*.' *Antimicrobial Agents and Chemotherapy*. American Society for Microbiology, 38(6) pp. 1256–1261.

Castillo, D.; Harcourt, B.; Hatcher, C.; Jackson, M.; Katz, L.; Mayer, L.; Novak, R.; Rahalison, L,; Schmink, S.; Theodore, J,; Thomas, J,; Vuong, J, Wang, X. (2011) 'Epidemiology of meningitis caused by *Neisseria meningitidis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*.' *Laboratory methods for the diagnosis of meningitis* pp. 1–8.

Caugant, D. A. and Brynildsrud, O. B. (2020) '*Neisseria meningitidis*: using genomics to understand diversity, evolution and pathogenesis.' *Nature Reviews Microbiology*. Springer US, 18(2) pp. 84–96.

Caugant, D. A. and Maiden, M. C. J. (2009) 'Meningococcal carriage and disease-Population biology and evolution.' *Vaccine*, 27(SUPPL. 2).

Cehovin, A., Simpson, P. J., McDowell, M. A., Brown, D. R., Noschese, R., Pallett, M., Brady, J., Baldwin, G. S., Lea, S. M., Matthews, S. J. and Pelicic, V. (2013) 'Specific DNA recognition mediated by a type IV pilin.' *Proceedings of the National Academy of Sciences of the United States of America*, 110(8) pp. 3065–3070.

Centers for Disease Control and Prevention (2020) *Yellow book: Traveler's health*. [Online] [Accessed on 26th March 2021] https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/meningococcal-disease.

Centers for Diseases Control and Prevention, (CDC) (2019) *Meningococcal disease: technical and clinical information*. online (Accessed 04/08/2021). [Online] https://www.cdc.gov/meningococcal/clinical-info.html.

Ceyhan, M., Anis, S., Htun-Myint, L., Pawinski, R., Soriano-Gabarró, M. and Vyse, A. (2012)

‘Meningococcal disease in the Middle East and North Africa: An important public health consideration that requires further attention.’ *International Journal of Infectious Diseases*, 16(8) pp. 574–582.

Ceyhan, M., Celik, M., Demir, E. T., Gurbuz, V., Aycan, A. E. and Unal, S. (2013) ‘Acquisition of meningococcal serogroup W-135 carriage in turkish hajj pilgrims who had received the quadrivalent meningococcal polysaccharide vaccine.’ *Clinical and Vaccine Immunology*, 20(1) pp. 66–68.

Chen, Mingliang, Guo, Q., Wang, Y., Zou, Y., Wang, G., Zhang, X., Xu, X., Zhao, M., Hu, F., Qu, D., Chen, Min and Wang, M. (2015) ‘Shifts in the antibiotic susceptibility, serogroups, and clonal complexes of *Neisseria meningitidis* in Shanghai, China: A time trend analysis of the pre-quinolone and quinolone eras.’ *PLoS Medicine*. Public Library of Science, 12(6) pp. 1–22.

Chen, Mingliang, Zhang, C., Zhang, X. and Chen, Min (2020) ‘Meningococcal quinolone resistance originated from several commensal *Neisseria* species.’ *Antimicrobial Agents and Chemotherapy*, 64(2) pp. 1–12.

Christensen, H., May, M., Bowen, L., Hickman, M. and Trotter, C. L. (2010) ‘Meningococcal carriage by age: A systematic review and meta-analysis.’ *The Lancet Infectious Diseases*. Elsevier Ltd, 10(12) pp. 853–861.

Clark, S. A., Lucidarme, J., Newbold, L. S. and Borrow, R. (2014) ‘Genotypic Analysis of Meningococcal Factor H-Binding Protein from Non-Culture Clinical Specimens.’ *PLOS ONE*. Public Library of Science, 9(2) pp. 1–8.

Clinical and Laboratory Standards Institute (2015) *M07-A10: Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; Approved standard—tenth edition.* CLSI (Clinical and Laboratory Standards Institute). [Online] [Accessed on 26th March 2021] https://clsi.org/media/1632/m07a10_sample.pdf.

Clinical and Laboratory Standards Institute (2019) *Performance standards for antimicrobial susceptibility testing. 29th Edition, CLSI supplement M100.* [Online] [Accessed on 26th March 2021] https://clsi.org/standards/products/microbiology/documents/m100/.

Colicchio, R., Pagliuca, C., Pastore, G., Cicatiello, A. G., Pagliarulo, C., Talà, A., Scaglione, E., Sammartino, J. C., Bucci, C., Alifano, P. and Salvatore, P. (2015) 'Fitness cost of rifampin resistance in *Neisseria meningitidis*: In Vitro study of mechanisms associated with *rpoB* H553Y mutation.' *Antimicrobial Agents and Chemotherapy*, 59(12) pp. 7637–7649.

Coureuil, M., Join-Lambert, O., Lécuyer, H., Bourdoulous, S., Marullo, S. and Nassif, X. (2012) 'Mechanism of meningeal invasion by *Neisseria meningitidis*.' *Virulence*, 3(2) pp. 164–172.

Davies, J & Davies, D. (2010) 'Origins and evolution of antibiotic resistance.' *Microbiology and molecular biology reviews : MMBR*, 74(3) pp. 417–433.

Dawson, S., Fey, R. and McNulty, C. (1999) 'Meningococcal disease in siblings caused by rifampicin sensitive and rifampicin resistant strains.' *Communicable Disease and Public Health*, 2(3) pp. 215–216.

Deghmane, A. E., Hong, E. and Taha, M. K. (2017) 'Emergence of meningococci with reduced susceptibility to third-generation cephalosporins.' *Journal of Antimicrobial Chemotherapy*. Oxford University Press, 72(1) pp. 95–98.

Deghmane, A. E., Hong, E. and Taha, M. K. (2018) 'Acquisition of beta-lactamase by *Neisseria meningitidis* through possible horizontal gene transfer.' *Journal of Antimicrobial Chemotherapy*. Oxford University Press, 62(9) pp. 1–3.

Didelot, X. and Maiden, M. C. J. (2010) 'Impact of recombination on bacterial evolution.' *Trends in microbiology*. 2010/05/06, 18(7) pp. 315–322.

Diggle, M. A. and Clarke, S. C. (2003) 'Detection and genotyping of meningococci using a nested PCR approach.' *Journal of Medical Microbiology*, 52(1) pp. 51–57.

Dillon, J. R., Yei, K.-H., Pauzé, M. and Yeung, K.-H. (1983) 'Spread of penicillinase-producing and transfer plasmids from the gonococcus to *Neisseria meningitidis*.' *The Lancet*. Elsevier, 321(8328) pp. 779–781.

Djingarey, M. H., Diomandé, F. V. K., Barry, R., Kandolo, D., Shirehwa, F., Lingani, C., Novak, R. T., Tevi-Benissan, C., Perea, W., Preziosi, M.-P. and LaForce, F. M. (2015) 'Introduction and rollout of a new group A meningococcal conjugate vaccine (PsA-TT) in

African meningitis belt countries, 2010–2014.' *Clinical Infectious Diseases*, 61(suppl_5) pp. S434–S441.

Drlica, K. and Zhao, X. (1997) 'DNA gyrase, topoisomerase IV, and the 4-quinolones.' *Microbiology and molecular biology reviews : MMBR*, 61(3) pp. 377–92.

Ehlenberger, A. G. and Nussenzweig, V. (1977) 'The role of membrane receptors for C3b and C3d in phagocytosis.' *Journal of Experimental Medicine*, 145(C) pp. 357–371.

Eriksson, J., Eriksson, O. S., Maudsdotter, L., Palm, O., Engman, J., Sarkissian, T., Aro, H., Wallin, M. and Jonsson, A.-B. (2015) 'Characterization of motility and piliation in pathogenic *Neisseria*.' *BMC microbiology*. BioMed Central, 15 p. 92.

Van Esso, D., Fontanals, D., Uriz, S., Morera, M. A., Juncosa, T., Latorre, C. and Duran, M. (1987) '*Neisseria meningitidis* strains with decreased susceptibility to penicillin.' *The Pediatric infectious disease journal*. United States, 8(5) pp. 438–439.

European Centre for Disease Prevention and Control (2017) 'Invasive meningococcal disease annual epidemiological report for 2017.' *Annual epidemiological report on communicable diseases in Europe* pp. 1–10.

European Centre for Diseases Prevention and Control (2013) *Surveillance of invasive bacterial diseases in Europe, 2011*. Stockholm: ECDC. [Online] https://www.ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/Surveillance of IBD in Europe 2012.pdf.

European Committee on Antimicrobial Susceptibility Testing (2019) *New definitions of S, I and R from 2019*. [Online] [Accessed on 26th March 2021] https://www.eucast.org/newsiandr/.

Fernandez, K., Lingani, C., Aderinola, O. M., Goumbi, K., Bicaba, B., Edea, Z. A., Glèlè, C., Sarkodie, B., Tamekloe, A., Ngomba, A., Djingarey, M., Bwaka, A., Perea, W. and Ronveaux, O. (2019) 'Meningococcal meningitis outbreaks in the African meningitis belt after meningococcal serogroup A conjugate vaccine introduction, 2011-2017.' *Journal of Infectious Diseases*, 220(Suppl 4) pp. S225–S232.

Figueroa, J., Andreoni, J. and Densen, P. (1993) 'Complement deficiency states and

meningococcal disease.' *Immunologic research*. United States, 12(3) pp. 295–311.

Fine, A., Layton, M., Hakim, A. and Smith, P. (2000) 'Serogroup W-135 meningococcal disease among travelers returning From Saudi Arabia --- United States, 2000.' *Morbidity and Mortality Weekly Report*, 49(16) pp. 345–346.

Finne, J., Leinonen, M. and Makela, P. H. (1983) 'Antigenic similarities between brain components and bacteria causing meningitis. Implications for vaccine development and pathogenesis.' *Lancet*. England, 2(8346) pp. 355–357.

Fleming, A. (1929) 'On the antibacterial action of cultures of a penicillium, with special reference to their use in the isolation of *B. influenzæ*.' *British journal of experimental pathology* pp. 226–236.

Fontanals, D., Pineda, V., Pons, I. and Rojo, J. C. (1989) 'Penicillin-resistant beta-lactamase producing *Neisseria meningitidis* in Spain.' *European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology*. Germany pp. 90–91.

Gold, R. and Artenstein, M. S. (1971) 'Meningococcal infections. 2. Field trial of group C meningococcal polysaccharide vaccine in 1969-70.' *Bulletin of the World Health Organization*, 45(3) pp. 279–282.

Gold, R., Lepow, M. L., Goldschneider, I., Draper, T. F. and Gotschlich, E. C. (1979) 'Kinetics of antibody production to group A and group C meningococcal polysaccharide vaccines administered during the first six years of life: Prospects for routine immunization of infants and children.' *The Journal of Infectious Diseases*, 140(5) pp. 690–697.

Gold, R., Lepow, M. L., Goldschneider, I., Draper, T. L. and Gotschlich, E. C. (1975) 'Clinical evaluation of group A and group C meningococcal polysaccharide vaccines in infants.' *The Journal of Clinical Investigation*, 56 pp. 1536–1547.

Goldschneider, I., Gotschlich, E. C. and Artenstein, M. S. (1969a) 'Human immunity to the meningococcus. I. The role of humoral antibodies.' *The Journal of experimental medicine*, 129(6) pp. 1307–1326.

Goldschneider, I., Gotschlich, E. C. and Artenstein, M. S. (1969b) 'Human immunity to the

meningococcus. II. Development of natural immunity.' *The Journal of experimental medicine*, 129(6) pp. 1327–1348.

Goodman, S. and Scocca, J. (1988) 'Identification and arrangement of the DNA sequence recognized in specific transformation of *Neisseria gonorrhoeae*.' *Proceedings of the National Academy of Sciences*, 85(18) pp. 6982–6986.

Gorla, Maria Cecília, Cassiolato, A. P., Pinhata, J. M. W., De Moraes, C., Corso, A., Gagetti, P. and Lemos, A. P. (2018) 'Emergence of resistance to ciprofloxacin in *Neisseria meningitidis* in Brazil.' *Journal of Medical Microbiology*. Microbiology Society, 67(3) pp. 286–288.

Gorla, Maria Cecilia, Pinhata, J. M. W., Dias, U. J., de Moraes, C. and Lemos, A. P. (2018) 'Surveillance of antimicrobial resistance in *Neisseria meningitidis* strains isolated from invasive cases in Brazil from 2009 to 2016.' *Journal of medical microbiology*. England, 67(6) pp. 750–756.

Gray, S. J., Trotter, C. L., Ramsay, M. E., Guiver, M., Fox, A. J., Borrow, R., Mallard, R. H. and Kaczmarski, E. B. (2006) 'Epidemiology of meningococcal disease in England and Wales 1993/94 to 2003/04: contribution and experiences of the Meningococcal Reference Unit.' *Journal of medical microbiology*. England, 55(Pt 7) pp. 887–896.

Hackett, S. J., Carrol, E. D., Guiver, M., Marsh, J., Sills, J. A., Thomson, A. P. J., Kaczmarski, E. B. and Hart, C. A. (2002) 'Improved case confirmation in meningococcal disease with whole blood Taqman PCR.' *Archives of disease in childhood*. England, 86(6) pp. 449–452.

Hagman, K. E., Pan, W., Spratt, B. G., Balthazar, J. T., Judd, R. C. and Shafer, W. M. (1995) 'Resistance of *Neisseria gonorrhoeae* to antimicrobial hydrophobic agents is modulated by the mtrRCDE efflux system.' *Microbiology*, 141(3) pp. 611–622.

Hahné, S. J. M., Charlett, A., Purcell, B., Samuelsson, S., Camaroni, I., Ehrhard, I., Heuberger, S., Santamaria, M. and Stuart, J. M. (2005) 'Mortality from meningococcal disease : Systematic review,' (January 1983) pp. 1–5.

Hall, T. (1999) 'BioEdit: a user-friendly biological sequence alignment editor and analysis program for Windows 95/98/NT.' *Nucleic Acids Symposium Series*, 41 pp. 95–98.

Halperin, S. A., Bettinger, J. A., Greenwood, B., Harrison, L. H., Jelfs, J., Ladhani, S. N., McIntyre, P., Ramsay, M. E. and Sáfadi, M. A. P. (2012) 'The changing and dynamic epidemiology of meningococcal disease.' *Vaccine*. Elsevier Ltd, 30(SUPPL. 2) pp. B26–B36.

Hansman, D. (1983) 'Meningococcal disease in South Australia: incidence and serogroup distribution 1971–1980.' *Journal of Hygiene*. 2009/10/19, Cambridge University Press, 90(1) pp. 49–54.

Harrison, Odile B, Cole, K., Peters, J., Cresswell, F., Dean, G., Eyre, D. W., Paul, J. and Maiden, M. C. (2017) 'Genomic analysis of urogenital and rectal *Neisseria meningitidis* isolates reveals encapsulated hyperinvasive meningococci and coincident multidrug-resistant gonococci.' *Sexually transmitted infections*, 93(6) pp. 445–451.

Harrison, Odile B., Schoen, C., Retchless, A. C., Wang, X., Jolley, K. A., Bray, J. E. and Maiden, M. C. J. (2017) '*Neisseria* genomics: Current status and future perspectives.' *Pathogens and Disease*, 75(6) pp. 1–11.

Hart, C. A. and Thomson, A. P. J. (2006) 'Meningococcal disease and its management in children.' *British Medical Journal*, 333(7570) pp. 685–690.

Hartmann, G., Honikel, K. O., Knusel, F. and Nuesch, J. (1967) 'The specific inhibition of the DNA-directed RNA synthesis by rifamycin.' *Biochimica et biophysica acta*. Netherlands, 145(3) pp. 843–844.

Hawkins, K., Hoffman, M., Okuyama, S. and Rowan, S. (2017) 'A case of fulminant meningococcemia: It is all in the complement.' *BMJ Case Reports*, 2017 pp. 1–3.

Heckenberg, S. G. B., De Gans, J., Brouwer, M. C., Weisfelt, M., Piet, J. R., Spanjaard, L., Van Der Ende, A. and Van De Beek, D. (2008) 'Clinical features, outcome, and meningococcal genotype in 258 adults with meningococcal meningitis: A prospective cohort study.' *Medicine*, 87(4) pp. 185–192.

Hedberg, S. T., Fredlund, H., Nicolas, P., Caugant, D. A., Olcén, P. and Unemo, M. (2009) 'Antibiotic susceptibility and characteristics of *Neisseria meningitidis* isolates from the African meningitis belt, 2000 to 2006: Phenotypic and genotypic perspectives.' *Antimicrobial Agents and Chemotherapy*, 53(4) pp. 1561–1566.

Heinsbroek, E., Ladhani, S., Gray, S., Guiver, M., Kaczmarski, E., Borrow, R. and Ramsay, M. (2013) 'Added value of PCR-testing for confirmation of invasive meningococcal disease in England.' *Journal of Infection*, 67(5) pp. 385–390.

Hellenbrand, W., Koch, J., Harder, T., Bogdan, C., Heininger, U., Tenenbaum, T., Terhardt, M., Vogel, U., Wichmann, O. and von Kries, R. (2015) 'Background paper for the update of meningococcal vaccination recommendations in Germany: use of the serogroup B vaccine in persons at increased risk for meningococcal disease.' *Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz*, 58(11–12) pp. 1314–1343.

Hillmen, P., Young, N. S., Schubert, J., Brodsky, R. A., Socié, G., Muus, P., Röth, A., Szer, J., Elebute, M. O., Nakamura, R., Browne, P., Risitano, A. M., Hill, A., Schrezenmeier, H., Fu, C. L., Maciejewski, J., Rollins, S. A., Mojcik, C. F., Rother, R. P. and Luzzatto, L. (2006) 'The complement inhibitor eculizumab in paroxysmal nocturnal hemoglobinuria.' *New England Journal of Medicine*, 355(12) pp. 1233–1243.

Hoang, L. M. N., Thomas, E., Tyler, S., Pollard, A. J., Stephens, G., Gustafson, L., McNabb, A., Pocock, I., Tsang, R. and Tan, R. (2005) 'Rapid and fatal meningococcal disease due to a strain of *Neisseria meningitidis* containing the capsule null locus.' *Clinical Infectious Diseases*, 40(5) pp. e38–e42.

Hong, E., Thulin Hedberg, S., Abad, R., Fazio, C., Enríquez, R., Deghmane, A. E., Jolley, K. A., Stefanelli, P., Unemo, M., Vazquez, J. A., Veyrier, F. J. and Taha, M. K. (2013) 'Target gene sequencing to define the susceptibility of *Neisseria meningitidis* to ciprofloxacin.' *Antimicrobial Agents and Chemotherapy*, 57(4) pp. 1961–1964.

Hooper, D. C. (2001) 'Emerging mechanisms of fluoroquinolone resistance.' *Emerging infectious diseases*, 7(2) pp. 337–341.

Huson, D. H. (1998) 'SplitsTree: Analyzing and visualizing evolutionary data.' *Bioinformatics*. Oxford University Press, 14(1) pp. 68–73.

Ikeda, F., Tsuji, A., Kaneko, Y., Nishida, M. and Goto, S. (1986) 'Conjugal transfer of beta-lactamase-producing plasmids of *Neisseria gonorrhoeae* to *Neisseria meningitidis*.' *Microbiology and immunology*. Australia, 30(8) pp. 737–742.

Jackson, L. and Wenger, J. (1993) 'Laboratory-based surveillance for meningococcal

disease in selected Areas, United States, 1989-1991,' 42 pp. 21–30.

Jeanteur, D., Lakey, J. H. and Pattus, F. (1991) 'The bacterial porin superfamily: sequence alignment and structure prediction.' *Molecular microbiology*. England, 5(9) pp. 2153–2164.

Jiang, H.-Q., Hoiseth, S. K., Harris, S. L., McNeil, L. K., Zhu, D., Tan, C., Scott, A. A., Alexander, K., Mason, K., Miller, L., DaSilva, I., Mack, M., Zhao, X.-J., Pride, M. W., Andrew, L., Murphy, E., Hagen, M., French, R., Arora, A., Jones, T. R., Jansen, K. U., Zlotnick, G. W. and Anderson, A. S. (2010) 'Broad vaccine coverage predicted for a bivalent recombinant factor H binding protein based vaccine to prevent serogroup B meningococcal disease.' *Vaccine*. Netherlands, 28(37) pp. 6086–6093.

Jodar, L., Feavers, I. M., Salisbury, D. and Granoff, D. M. (2002) 'Development of vaccines against meningococcal disease.' *Lancet (London, England)*. England, 359(9316) pp. 1499–1508.

Jolley, K. A., Brehony, C. and Maiden, M. C. J. (2007) 'Molecular typing of meningococci: recommendations for target choice and nomenclature.' *FEMS microbiology reviews*. England, 31(1) pp. 89–96.

Jolley, K. A., Chan, M. S. and Maiden, M. C. J. (2004) 'mlstdbNet - Distributed multi-locus sequence typing (MLST) databases.' *BMC Bioinformatics*, 5 pp. 1–8.

Jolley, K. A. and Maiden, M. C. J. (2010) 'BIGSdb: Scalable analysis of bacterial genome variation at the population level.' *BMC Bioinformatics*. BioMed Central Ltd, 11(1) p. 595.

Jones, D. M. and Sutcliffe, E. M. (1990) 'Meningococci with reduced susceptibility to penicillin.' *Lancet (London, England)*. England pp. 863–864.

De Jonge, M. I., Bos, M. P., Hamstra, H. J., Jiskoot, W., Van Ulsen, P., Tommassen, J., Van Alphen, L. and Van Der Ley, P. (2002) 'Conformational analysis of opacity proteins from *Neisseria meningitidis*.' *European Journal of Biochemistry*, 269(21) pp. 5215–5223.

Joyce, M., Laing, A., Mullet, H., Gilmore, M. F. and Cormican, M. (2003) 'Isolated septic arthritis: meningococcal infection.' *Journal of the Royal Society of Medicine*. The Royal Society of Medicine, 96(5) pp. 237–238.

Kawasaki, Y., Matsubara, K., Takahashi, H., Morita, M., Ohnishi, M., Hori, M., Isome, K., Iwata, A., Nigami, H., Ikemachi, M., Yamamoto, G. and Ohkusu, K. (2018) 'Invasive meningococcal disease due to ciprofloxacin-resistant *Neisseria meningitidis* sequence type 4821: The first case in Japan.' *Journal of Infection and Chemotherapy*. Elsevier B.V., 24(4) pp. 305–308.

Khatami, A., Peters, A., Robinson, H., Williams, N., Thompson, A., Findlow, H., Pollard, A. J. and Snape, M. D. (2011) 'Maintenance of immune response throughout childhood following serogroup C meningococcal conjugate vaccination in early childhood.' *Clinical and Vaccine Immunology*, 18(12) pp. 2038–2042.

Knol, M. J., Hahné, S. J. M., Lucidarme, J., Campbell, H., de Melker, H. E., Gray, S. J., Borrow, R., Ladhani, S. N., Ramsay, M. E. and van der Ende, A. (2017) 'Temporal associations between national outbreaks of meningococcal serogroup W and C disease in the Netherlands and England: an observational cohort study.' *The Lancet Public Health*. Elsevier Ltd, 2(10) pp. e473–e482.

Kong, K.-F., Schneper, L. and Mathee, K. (2010) 'Beta-lactam antibiotics: from antibiosis to resistance and bacteriology.' *APMIS : acta pathologica, microbiologica, et immunologica Scandinavica*, 118(1) pp. 1–36.

Köser, C. U., Ellington, M. J., Cartwright, E. J. P., Gillespie, S. H., Brown, N. M., Farrington, M., Holden, M. T. G., Dougan, G., Bentley, S. D., Parkhill, J. and Peacock, S. J. (2012) 'Routine use of microbial whole genome sequencing in diagnostic and public health microbiology.' *PLoS Pathogens*, 8(8) pp. 1–9.

Koumaré, B., Ouedraogo-Traoré, R., Sanou, I., Yada, A. A., Sow, I., Lusamba, P. S., Traoré, E., Dabal, M., Santamaria, M., Hacen, M. M., Kaboré, A. B. and Caugant, D. A. (2007) 'The first large epidemic of meningococcal disease caused by serogroup W135, Burkina Faso, 2002.' *Vaccine*, 25(SUPPL. 1) pp. 37–41.

Kvalsvig, A. J. and Unsworth, D. J. (2003) 'The immunopathogenesis of meningococcal disease.' *Journal of Clinical Pathology*, 56(6) pp. 417–422.

Ladhani, S. N., Andrews, N., Parikh, S. R., Campbell, H., White, J., Edelstein, M., Bai, X., Lucidarme, J., Borrow, R. and Ramsay, M. E. (2020) 'Vaccination of infants with

meningococcal group B vaccine (4CMenB) in England.' *New England Journal of Medicine*, 382(4) pp. 309–317.

Ladhani, S. N., Campbell, H., Lucidarme, J., Gray, S., Parikh, S., Willerton, L., Clark, S. A., Lekshmi, A., Walker, A., Patel, S., Bai, X., Ramsay, M. and Borrow, R. (2019) 'Invasive meningococcal disease in patients with complement deficiencies: a case series (2008-2017).' *BMC infectious diseases*. BioMed Central, 19(1) p. 522.

Lapadula, G., Viganò, F., Fortuna, P., Dolara, A., Bramati, S., Soria, A., Foresti, S. and Gori, A. (2009) 'Imported ciprofloxacin-resistant *Neisseria meningitidis*.' *Emerging infectious diseases* pp. 1852–1854.

Legendre, C. M., Licht, C., Muus, P., Greenbaum, L. A., Babu, S., Bedrosian C Bingham, C., Cohen, D. J., Delmas, Y., Douglas, K., Eitner, F., Feldkamp, T., Fouque, D., Furman, R. R., Gaber, O., Herthelius, M., Hourmant, M., Karpman, D., Lebranchu, Y., Mariat, C., Menne, J., Moulin, B., Nürnberger, J., Ogawa, M., Remuzzi, G., Richard, T., Sberro-Soussan, R., Severino, B., Sheerin, N. S., Trivelli, A., Zimmerhackl, L. B., Goodship, T. and Loirat, C. (2013) 'Terminal complement inhibitor eculizumab in atypical hemolytic-uremic syndrome.' *New England Journal of Medicine*, 368(23) pp. 2169–2181.

Lewis, L. A. and Ram, S. (2014) 'Meningococcal disease and the complement system.' *Virulence*, 5(1) pp. 98–126.

Lin, E. Y., Adamson, P. C. and Klausner, J. D. (2021) 'Epidemiology, treatments, and vaccine development for antimicrobial-resistant *Neisseria gonorrhoeae*: Current strategies and future directions.' *Drugs*. Springer International Publishing, 81(10) pp. 1153–1169.

Lindberg, R., Fredlund, H., Nicholas, R. and Unemo, M. (2007) '*Neisseria gonorrhoeae* isolates with reduced susceptibility to cefixime and ceftriaxone: association with genetic polymorphisms in *penA, mtrR, porB1b*, and *ponA*.' *Antimicrobial Agents and Chemotherapy*, 51(6) pp. 2117 LP – 2122.

Lingappa, J., Al-Rabeah, A., Hajjeh, R., Mustafa, T., Fatani, A., Al-Bassam, T., Budukhan, A., Turkistani, A. M., Al-Hamdam, N., Al-Jeffri, M., Mazrou, Y., Perkins, B., Popovic, T., Mayer, L. and Rosenstein, N. (2003) 'Serogroup W-135 meningococcal disease during the Hajj,

2000.' *Emerging Infectious Diseases*, 9(6) pp. 666–671.

Liu, G., Tang, C. M. and Exley, R. M. (2015) 'Non-pathogenic *Neisseria*: members of an abundant, multi-habitat, diverse genus.' *Microbiology (Reading, England)*. England, 161(7) pp. 1297–1312.

Lopardo, H. A., Santander, C., Ceinos, M. D. C. and Rubeglio, E. A. (1993) 'Isolation of moderately penicillin-susceptible strains of *Neisseria meningitidis* in Argentina.' *Antimicrobial Agents and Chemotherapy*, 37(8) pp. 1728–1729.

Lucidarme, J., Hill, D. M. C., Bratcher, H. B., Gray, S. J., du Plessis, M., Tsang, R. S. W., Vazquez, J. A., Taha, M. K., Ceyhan, M., Efron, A. M., Gorla, M. C., Findlow, J., Jolley, K. A., Maiden, M. C. J. and Borrow, R. (2015) 'Genomic resolution of an aggressive, widespread, diverse and expanding meningococcal serogroup B, C and W lineage.' *Journal of Infection*. W.B. Saunders Ltd, 71(5) pp. 544–552.

Lucidarme, J., Scott, K. J., Ure, R., Smith, A., Lindsay, D., Stenmark, B., Jacobsson, S., Fredlund, H., Cameron, J. C., Smith-Palmer, A., McMenamin, J., Gray, S. J., Campbell, H., Ladhani, S., Findlow, J., Molling, P. and Borrow, R. (2016) 'An international invasive meningococcal disease outbreak due to a novel and rapidly expanding serogroup W strain, Scotland and Sweden, July to August 2015.' *Eurosurveillance*. European Centre for Disease Prevention and Control (ECDC), 21(45) pp. 1–9.

Lucidarme, J., Tan, L., Exley, R. M., Findlow, J., Borrow, R. and Tang, C. M. (2011) 'Characterization of *Neisseria meningitidis* isolates that do not express the virulence factor and vaccine antigen factor H binding protein.' *Clinical and vaccine immunology : CVI*, 18(6) pp. 1002–1014.

Madico, G., Welsch, J. A., Lewis, L. A., McNaughton, A., Perlman, D. H., Costello, C. E., Ngampasutadol, J., Vogel, U., Granoff, D. M. and Ram, S. (2006) 'The meningococcal vaccine candidate GNA1870 binds the complement regulatory protein factor H and enhances serum resistance.' *The Journal of Immunology*, 177(1) p. 501.

Maiden, M. C. J., Bygraves, J. A., Feil, E., Morelli, G., Russell, J. E., Urwin, R., Zhang, Q., Zhou, J., Zurth, K., Caugant, D. A., Feavers, I. M., Achtman, M. and Spratt, B. G. (1998) 'Multilocus sequence typing: A portable approach to the identification of clones within

populations of pathogenic microorganisms.' *Proceedings of the National Academy of Sciences of the United States of America*, 95(6) pp. 3140–3145.

Maiden, M. C. J., Jansen van Rensburg, M., Bray, J. E., Earle, S., Ford, S., Jolley, K. A. and McCarthy, N. (2013) 'MLST revisitied: the gene-by-gene approach to bacterial genomics.' *Nature Reviews Microbiology*, 11(10) pp. 728–736.

Manchanda, V. and Bhalla, P. (2006) 'Emergence of non-ceftriaxone-susceptible *Neisseria meningitidis* in India.' *Journal of clinical microbiology* pp. 4290–4291.

Maness, M. J. and Sparling, P. F. (1973) 'Multiple antibiotic resistance due to a single mutation in *Neisseria gonorrhoeae*.' *The Journal of Infectious Diseases*, 128(3) pp. 321–330.

Martin, D. R., Walker, S. J., Baker, M. G. and Lennon, D. R. (1998) 'New Zealand epidemic of meningococcal disease identified by a strain with phenotype B:4:P1.4.' *The Journal of infectious diseases*. United States, 177(2) pp. 497–500.

Martin, N. V., Ong, K. S., Howden, B. P., Lahra, M. M., Lambert, S. B., Beard, F. H., Dowse, G. K. and Saul, N. (2016) 'Rise in invasive serogroup W meningococcal disease in Australia 2013-2015.' *Communicable diseases intelligence quarterly report*, 40(4) pp. E454–E459.

Maslow, M. J. and Portal-Celhay, C. (2015) 'Rifamycins.' *In* Bennett, J. E., Dolin, R., and Blaser Douglas, and Bennett's Principles and Practice of Infectious Diseases (Eighth Edition), M. J. B. T.-M. (eds). Philadelphia: W.B. Saunders, pp. 339-349.e3.

McNamara, L. A., Potts, C., Blain, A. E., Retchless, A. C., Reese, N., Swint, S., Lonsway, D., Karlsson, M., Lunquest, K., Sweitzer, J. J., Wang, X., Hariri, S. and Fox, L. A. M. (2020) 'Detection of ciprofloxacin-resistant, β-lactamase-producing *Neisseria meningitidis* serogroup Y isolates - United States, 2019-2020.' *MMWR. Morbidity and mortality weekly report*, 69(24) pp. 735–739.

McNamara, L. A., Potts, C. C., Blain, A., Topaz, N., Apostol, M., Muse, A., Poissant, T., Wang, X. and Macneil, J. R. (2016) 'Invasive meningococcal disease due to nongroupable *Neisseria meningitidis* — active bacterial core curveillance sites, 2011-2016' pp. 1–4.

McNamara, L. A., Topaz, N., Wang, X., Hariri, S., Fox, L. and Macneil, J. R. (2017) 'High risk

for invasive meningococcal disease among patients receiving eculizumab (Soliris) despite receipt of meningococcal vaccine.' *Morbidity and Mortality Weekly Report*, 66(27) pp. 734–737.

Memish, Z. A., Al-Tawfiq, J. A., Almasri, M., Azhar, E. I., Yasir, M., Al-Saeed, M. S., Ben Helaby, H., Borrow, R., Turkistani, A. and Assiri, A. (2017) '*Neisseria meningitidis* nasopharyngeal carriage during the Hajj: A cohort study evaluating the need for ciprofloxacin prophylaxis.' *Vaccine*. Netherlands, 35(18) pp. 2473–2478.

Millar, B. C., Moore, P. J. A. and Moore, J. E. (2016) 'Meningococcal disease: Has the battle been won?' *Journal of the Royal Army Medical Corps*, 163(4) pp. 235–241.

Moore, P., Schwartz, B., Reeves, M., Gellin, B. and Broome, C. (1989) 'Intercontinental spread of an epidemic group A *Neisseria meningitidis* strain.' *The Lancet*. Elsevier, 334(8657) pp. 260–263.

Morgan, D. R., Spence, M., Crowe, M. and O'Keeffe, D. B. (2002) 'Primary (isolated) meningococcal pericarditis.' *Clinical Cardiology*, 25(6) pp. 305–307.

Mouton, R. P., Bongaerts, G. P. A. and Van Gestel, M. (1979) 'Comparison of activity and beta-lactamase stability of cefotaxime with those of six other cephalosporins.' *Antimicrobial Agents and Chemotherapy*, 16(6) pp. 757–760.

Mowlaboccus, S., Jolley, K. A., Bray, J. E., Pang, S., Lee, Y. T., Bew, J. D., Speers, D. J., Keil, A. D., Coombs, G. W. and Kahler, C. M. (2017) 'Clonal expansion of new penicillin-resistant clade of *Neisseria meningitidis* serogroup W clonal complex 11, Australia.' *Emerging Infectious Diseases*. Centers for Disease Control and Prevention (CDC), 23(8) pp. 1364–1367.

Mulhall, R. M., Bennett, D., Cunney, R., Borrow, R., Lucidarme, J., Findlow, J., Jolley, K. A., Bray, J., Maiden, M. C. J., Moschioni, M., Serino, L., Stella, M. and Medini, D. (2018) 'Potential coverage of the 4CMenB vaccine against invasive serogroup B *Neisseria meningitidis* isolated from 2009 to 2013 in the Republic of Ireland.' *mSphere*, 3(4) pp. 1–12.

Mustapha, M. M. and Harrison, L. H. (2018) 'Vaccine prevention of meningococcal disease in Africa: Major advances, remaining challenges.' *Human Vaccines and*

Immunotherapeutics. Taylor & Francis, 14(5) pp. 1107–1115.

Mustapha, M. M., Marsh, J. W. and Harrison, L. H. (2016) 'Global epidemiology of capsular group W meningococcal disease (1970-2015): Multifocal emergence and persistence of hypervirulent sequence type (ST)-11 clonal complex.' *Vaccine*. Elsevier Ltd, 34(13) pp. 1515–1523.

Nassif, X., Marceau, M., Pujol, C., Pron, B., Beretti, J. L. and Taha, M. K. (1997) 'Type-4 pili and meningococcal adhesiveness.' *Gene*, 192(1) pp. 149–153.

National Institute for Health and Care Excellence (2015) *Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management*. NICE Clinical guideline [CG102]. [Online] https://www.nice.org.uk/guidance/CG102/chapter/1-Guidance#pre-hospital-management-of-suspected-bacterial-meningitis-and-meningococcal-septicaemia.

Nester, C., Stewart, Z., Myers, D., Jetton, J., Nair, R., Reed, A., Thomas, C., Smith, R. and Brophy, P. (2011) 'Pre-emptive eculizumab and plasmapheresis for renal transplant in atypical hemolytic uremic syndrome.' *Clinical Journal of the American Society of Nephrology*, 6(6) pp. 1488–1494.

Nicolas, P. (2007) 'Emergence of non-ceftriaxone-susceptible *Neisseria meningitidis* in India.' *Journal of Clinical Microbiology*, 45(4) pp. 1378 LP – 1378.

Nicolas, P., Ait, N. M., Al-awaidy, S., Busaidy, S. AL, Sulaiman, N., Issa, M., Mahjour, J., Caugant, D. A., Olcé, P. N., Santamaria, M. and Busady, A. S. (2005) 'Pharyngeal carriage of serogroup W135 *Neisseria meningitidis* in Hajjees and their family contacts in Morocco, Oman and Sudan.' *APMIS*, 113 pp. 182–188.

Nolfi-Donegan, D., Konar, M., Vianzon, V., MacNeil, J., Cooper, J., Lurie, P., Sedivy, J., Wang, X., Granoff, D. M. and McNamara, L. (2018) 'Fatal nongroupable *Neisseria meningitidis* disease in vaccinated patient receiving eculizumab.' *Emerging Infectious Diseases*, 24(8) pp. 1561–1564.

Noone, D., Al-Matrafi, J., Tinckam, K., Zipfel, P. F., Herzenberg, A. M., Thorner, P. S., Pluthero, F. G., Kahr, W. H. A., Filler, G., Hebert, D., Harvey, E. and Licht, C. (2012) 'Antibody mediated rejection associated with complement factor H-related protein 3/1

deficiency successfully treated with Eculizumab.' *American Journal of Transplantation*, 12(9) pp. 2546–2553.

O'Neill, J. (2016) 'Tackling drug resistant infections globally: Final report and recommendations.'

Ohnishi, M., Saika, T., Hoshina, S., Iwasaku, K., Nakayama, S., Watanabe, H. and Kitawaki, J. (2011) 'Ceftriaxone-resistant *Neisseria gonorrhoeae*.' *Emerging infectious diseases* pp. 148–149.

Olbrich, K. J., Müller, D., Schumacher, S., Beck, E., Meszaros, K. and Koerber, F. (2018) 'Systematic review of invasive meningococcal disease: Sequelae and quality of life impact on patients and their caregivers.' *Infectious Diseases and Therapy*, 7(4) pp. 421–438.

Oppenheim, B. A. (1997) 'Antibiotic resistance in *Neisseria meningitidis*.' *Clinical Infectious Diseases*, 24(1) pp. 98–101.

Orden, B., Martínez, R., Millán, R., Belloso, M. and Pérez, N. (2003) 'Primary meningococcal conjunctivitis.' *Clinical Microbiology and Infection*, 9(12) pp. 1245–1247.

Pace, D. and Pollard, A. J. (2012) 'Meningococcal disease: Clinical presentation and sequelae.' *Vaccine*. Elsevier Ltd, 30(SUPPL. 2) pp. B3–B9.

Parikh, S. R., Andrews, N. J., Beebeejaun, K., Campbell, H., Ribeiro, S., Ward, C., White, J. M., Borrow, R., Ramsay, M. E. and Ladhani, S. N. (2016) 'Effectiveness and impact of a reduced infant schedule of 4CMenB vaccine against group B meningococcal disease in England: a national observational cohort study.' *The Lancet*. Elsevier Ltd, 388(10061) pp. 2775–2782.

Parikh, S. R., Campbell, H., Bettinger, J. A., Harrison, L. H., Marshall, H. S., Martinon-Torres, F., Safadi, M. A., Shao, Z., Zhu, B., von Gottberg, A., Borrow, R., Ramsay, M. E. and Ladhani, S. N. (2020) 'The everchanging epidemiology of meningococcal disease worldwide and the potential for prevention through vaccination.' *Journal of Infection*, 81(4) pp. 483–498.

Parikh, S. R., Lucidarme, J., Bingham, C., Warwicker, P., Goodship, T., Borrow, R. and Ladhani, S. N. (2017) 'Meningococcal B vaccine failure with a penicillin-resistant strain in a

young adult on long-term eculizumab.' *Pediatrics*. American Academy of Pediatrics (AAP), 140(3) pp. 1–4.

Parkhill, J., Achtman, M., James, K. D., Bentley, S. D., Churcher, C., Klee, S. R., Morelli, G., Basham, D., Brown, D., Chillingworth, T., Davies, R. M., Davis, P., Devlin, K., Feltwell, T., Hamlin, N., Holroyd, S., Jagels, K., Leather, S., Moule, S., Mungall, K., Quall, M. A., Rajandream, M. A., Rutherford, K. M., Simmonds, M., Skelton, J., Whitehead, S., Spratt, B. G. and Barrell, B. G. (2000) 'Complete DNA sequence of a serogroup A strain of *Neisseria meningitidis* Z2491.' *Nature*, 404(6777) pp. 502–506.

Peltola, H., Makela, H., Kayhty, H., Jousimies, H., Herva, E., Hallstrom, K., Sivonen, A., Renkonen, O. V, Pettay, O., Karanko, V., Ahvonen, P. and Sarna, S. (1977) 'Clinical efficacy of meningococcus group A capsular polysaccharide vaccine in children three months to five years of age.' *The New England journal of medicine*. United States, 297(13) pp. 686–691.

Pelton, S. I. (2016) 'The global evolution of meningococcal epidemiology following the introduction of meningococcal vaccines.' *Journal of Adolescent Health*. Elsevier Inc., 59(2) pp. S3–S11.

Perez, J. L., Absalon, J., Beeslaar, J., Balmer, P., Jansen, K. U., Jones, T. R., Harris, S., York, L. J., Jiang, Q., Radley, D., Anderson, A. S., Crowther, G. and Eiden, J. J. (2018) 'From research to licensure and beyond: clinical development of MenB-FHbp, a broadly protective meningococcal B vaccine.' *Expert Review of Vaccines*. Taylor & Francis, 17(6) pp. 461–477.

Peterson, E. and Kaur, P. (2018) 'Antibiotic resistance mechanisms in bacteria: Relationships between resistance determinants of antibiotic producers, environmental bacteria, and clinical pathogens.' *Frontiers in Microbiology*. Frontiers Media S.A., 9(2928) pp. 1–21.

Peterson, M. E., Mile, R., Li, Y., Nair, H. and Kyaw, M. H. (2018) 'Meningococcal carriage in high-risk settings: A systematic review.' *International Journal of Infectious Diseases*. Elsevier B.V., 73, August, pp. 109–117.

du Plessis, M., von Gottberg, A., Cohen, C., de Gouveia, L. and Klugman, K. P. (2008)

‘*Neisseria meningitidis* intermediately resistant to penicillin and causing invasive disease in South Africa in 2001 to 2005.’ *Journal of Clinical Microbiology*, 46(10) pp. 3208–3214.

Public Health England (2012) *Guidance for public health management of meningococcal disease in the UK. Updated August 2019*. Publich Health England. [Online] [Accessed on 26th March 2021] http://www.hpa.org.uk/webc/hpawebfile/hpaweb_c/1194947389261.

Public Health England (2019) *Ciprofloxacin resistant cases of non-groupable meningococcal infection connected to recent travel to Mecca*. *PHE Briefing Note*.

Rainbow, J., Cebelinski, E., Bartkus, J., Glennen, A., Boxrud, D. and Lynfield, R. (2005) ‘Rifampin-resistant meningococcal disease.’ *Emerging Infectious Diseases*, 11(6) pp. 977–979.

Retchless, A. C., Kretz, C. B., Chang, H.-Y., Bazan, J. A., Abrams, A. J., Norris Turner, A., Jenkins, L. T., Trees, D. L., Tzeng, Y.-L., Stephens, D. S., MacNeil, J. R. and Wang, X. (2018) ‘Expansion of a urethritis-associated *Neisseria meningitidis* clade in the United States with concurrent acquisition of *N. gonorrhoeae* alleles.’ *BMC genomics*. BioMed Central, 19(1) p. 176.

Riordan, F. A. I., Thomson, A. P. J., Sills, J. A. and Hart, C. (1995) ‘Bacterial meningitis in the first three months of life.’ *Postgraduate Medical Journal*, 71(831) pp. 36–38.

Rivero-Calle, I., Raguindin, P. F., Gómez-Rial, J., Rodriguez-Tenreiro, C. and Martinón-Torres, F. (2019) ‘Meningococcal group B vaccine for the prevention of invasive meningococcal disease caused by *Neisseria meningitidis* serogroup B.’ *Infection and drug resistance*, 12 pp. 3169–3188.

Roberts, M. C. (1989) ‘Plasmids of *Neisseria gonorrhoeae* and other *Neisseria* species.’ *Clinical Microbiology Reviews*, 2(SUPPL.) pp. 18–23.

Rodgers, E., Bentley, S. D., Borrow, R., Bratcher, H. B., Brisse, S., Brueggemann, A. B., Caugant, D. A., Findlow, J., Fox, L., Glennie, L., Harrison, L. H., Harrison, O. B., Heyderman, R. S., van Rensburg, M. J., Jolley, K. A., Kwambana-Adams, B., Ladhani, S., LaForce, M., Levin, M., Lucidarme, J., MacAlasdair, N., Maclennan, J., Maiden, M. C. J., Maynard-Smith, L., Muzzi, A., Oster, P., Rodrigues, C. M. C., Serino, O. R. L., Smith, V., van der Ende, A., Vázquez, J., Wang, X., Yezli, S. and Stuart, J. M. (2020) ‘The global meningitis genome

partnership.' *Journal of Infection*. Elsevier Ltd, (Published online ahead of print).

Rouphael N. G. and Stephens, D. S. (2012) '*Neisseria meningitidis*: biology, microbiology, and epidemiology.' *Methods Mol Biol*, 799 pp. 1–20.

Rouquette-Loughlin, C. E., Balthazar, J. T., Hill, S. A. and Shafer, W. M. (2004) 'Modulation of the mtrCDE-encoded efflux pump gene complex of *Neisseria meningitidis* due to a Correia element insertion sequence.' *Molecular Microbiology*, 54(3) pp. 731–741.

Sacchi, C., Lemos, A. P., Brandt, M. E., Whitney, A. M., Melles, C. E., Solari, C. A., Frasch, C. E. and Mayer, L. W. (1998) 'Proposed standardization of *Neisseria meningitidis* PorA variable-region typing nomenclature.' *Clinical and diagnostic laboratory immunology*. United States, 5(6) pp. 845–855.

Sacchi, C., Lemos, A. P. S., Whitney, A. M., Solari, C. A., Brandt, M. E., Melles, C. E. A., Frasch, C. E. and Mayer, L. W. (1998) 'Correlation between serological and sequencing analyses of the PorB outer membrane protein in the *Neisseria meningitidis* serotyping system.' *Clinical and Diagnostic Laboratory Immunology*, 5(3) pp. 348–354.

Sáez-Llorens, X. and McCracken, G. H. J. (1999) 'Antimicrobial and anti-inflammatory treatment of bacterial meningitis.' *Infectious disease clinics of North America*. United States, 13(3) pp. 619–36, vii.

Sáez-Nieto, J. A., Lujan, R., Berrón, S., Campos, J., Viñas, M., Fusté, C., Vazquez, J. A., Zhang, Q.-Y., Bowler, L. D., Martinez-Suarez, J. V and Spratt, B. G. (1992) 'Epidemiology and molecular basis of penicillin-resistant *Neisseria meningitidis* in Spain: A 5-year history (1985–1989).' *Clinical Infectious Diseases*, 14(2) pp. 394–402.

San Millan, A., Escudero, J. A., Catalan, A., Nieto, S., Farelo, F., Gibert, M., Moreno, M. A., Dominguez, L. and Gonzalez-Zorn, B. (2007) 'Beta-lactam resistance in *Haemophilus parasuis* is mediated by plasmid pB1000 bearing blaROB-1.' *Antimicrobial agents and chemotherapy*, 51(6) pp. 2260–2264.

San Millan, A., Garcia-Cobos, S., Escudero, J. A., Hidalgo, L., Gutierrez, B., Carrilero, L., Campos, J. and Gonzalez-Zorn, B. (2010) 'Haemophilus influenzae clinical isolates with plasmid pB1000 bearing blaROB-1: Fitness cost and interspecies dissemination.' *Antimicrobial Agents and Chemotherapy*, 54(4) pp. 1506–1511.

Santos-Neto, J. F., Ferreira, V. M., Feitosa, C. A., Martinez-Silveira, M. S. and Campos, L. C. (2019) 'Carriage prevalence of *Neisseria meningitidis* in the Americas in the 21st century: a systematic review.' *Brazilian Journal of Infectious Diseases*, 23(4) pp. 254–267.

Schneider, M. C., Exley, R. M., Ram, S., Sim, R. B. and Tang, C. M. (2007) 'Interactions between *Neisseria meningitidis* and the complement system.' *Trends in Microbiology*, 15(5) pp. 233–240.

Serruto, D., Bottomley, M. J., Ram, S., Giuliani, M. M. and Rappuoli, R. (2012) 'The new multicomponent vaccine against meningococcal serogroup B, 4CMenB: immunological, functional and structural characterization of the antigens.' *Vaccine*. Netherlands, 30 Suppl 2, May, pp. B87-97.

Shultz, T. R., Tapsall, J. W., White, P. A. and Newton, P. J. (2000) 'An invasive isolate of *Neisseria meningitidis* showing decreased susceptibility to quinolones.' *Antimicrobial agents and chemotherapy* p. 1116.

Singhal, S., Purnapatre, K. P., Kalia, V., Dube, S., Nair, D., Deb, M., Aggarwal, P., Gupta, S., Upadhyay, D. J., Rattan, A. and Raj, V. S. (2007) 'Ciprofloxacin-resistant *Neisseria meningitidis*, Delhi, India.' *Emerging Infectious Diseases*, 13(10) pp. 1614–1616.

Skoczyńska, A., Alonso, J.-M. and Taha, M. (2008) 'Ciprofloxacin resistance in *Neisseria meningitidis*, France.' *Emerging Infectious Diseases*. Centers for Disease Control and Prevention (CDC), 14(8) pp. 1322–1323.

Skoczynska, A., Ruckly, C., Hong, E. and Taha, M.-K. (2009) 'Molecular characterization of resistance to rifampicin in clinical isolates of *Neisseria meningitidis*.' *Clinical Microbiology and Infection*. Elsevier, 15(12) pp. 1178–1181.

Smith, I., Caugant, D. A., Høiby, E. A., Wentzel-Larsen, T. and Halstensen, A. (2006) 'High case-fatality rates of meningococcal disease in Western Norway caused by serogroup C strains belonging to both sequence type (ST)-32 and ST-11 complexes, 1985-2002.' *Epidemiology and Infection*, 134(6) pp. 1195–1202.

Sorhouet-Pereira, C., Efron, A., Gagetti, P., Faccone, D., Regueira, M., Corso, A., Gabastou, J. M. and Ibarz-Pavón, A. B. (2013) 'Phenotypic and genotypic characteristics of *Neisseria meningitidis* disease-causing strains in Argentina, 2010.' *PLoS ONE*, 8(3) pp. 1–7.

Spanjaard, L., Bol, P., de Marie, S. and Zanen, H. C. (1987) 'Association of meningococcal serogroups with the course of disease in the Netherlands, 1959-83.' *Bulletin of the World Health Organization*, 65(6) pp. 861–868.

Spinosa, M. R., Progida, C., Talà, A., Cogli, L., Alifano, P. and Bucci, C. (2007) 'The *Neisseria meningitidis* capsule is important for intracellular survival in human cells.' *Infection and immunity*, 75(7) pp. 3594–3603.

Spratt, B. G., Bowler, L. D., Zhang, Q. Y., Zhou, J. and Smith, J. M. (1992) 'Role of interspecies transfer of chromosomal genes in the evolution of penicillin resistance in pathogenic and commensal *Neisseria* species.' *Journal of Molecular Evolution*, 34(2) pp. 115–125.

Stefanelli, P., Fazio, C., La Rosa, G., Marianelli, C., Muscillo, M. and Mastrantonio, P. (2001) 'Rifampicin resistant meningococci causing invasive disease detection of point mutations in the *rpoB* gene.' *Journal of Antimicrobial Chemotherapy*, 47 pp. 219–212.

Struijk, G. H., Bouts, A. H. M., Rijkers, G. T., Kuin, E. A. C., Ten Berge, I. J. M. and Bemelman, F. J. (2013) 'Meningococcal sepsis complicating eculizumab treatment despite prior vaccination.' *American Journal of Transplantation*. Annals of Hematology, 13(3) pp. 819–820.

Taha, M.-K., Claus, H., Lappann, M., Veyrier, F. J., Otto, A., Becher, D., Deghmane, A.-E., Frosch, M., Hellenbrand, W., Hong, E., Parent du Chatelet, I., Prior, K., Harmsen, D. and Vogel, U. (2016) 'Evolutionary events associated with an outbreak of meningococcal disease in men who have sex with men.' *PloS one*. United States, 11(5) pp. 1–11.

Taha, M. K., Hedberg, S. T., Szatanik, M., Hong, E., Ruckly, C., Abad, R., Bertrand, S., Carion, F., Claus, H., Corso, A., Enríquez, R., Heuberger, S., Hryniewicz, W., Jolley, K. A., Kriz, P., Mollerach, M., Musilek, M., Neri, A., Olcén, P., Pana, M., Skoczynska, A., Pereira, C. S., Stefanelli, P., Tzanakaki, G., Unemo, M., Vázquez, J. A., Vogel, U. and Wasko, I. (2010) 'Multicenter study for defining the breakpoint for rifampin resistance in *Neisseria meningitidis* by *rpoB* sequencing.' *Antimicrobial Agents and Chemotherapy*, 54(9) pp. 3651–3658.

Taha, M. K., Vázquez, J. A., Hong, E., Bennett, D. E., Bertrand, S., Bukovski, S., Cafferkey,

M. T., Carion, F., Christensen, J. J., Diggle, M., Edwards, G., Enríquez, R., Fazio, C., Frosch, M., Heuberger, S., Hoffmann, S., Jolley, K. A., Kadlubowski, M., Kechrid, A., Kesanopoulos, K., Kriz, P., Lambertsen, L., Levenet, I., Musilek, M., Paragi, M., Saguer, A., Skoczynska, A., Stefanelli, P., Thulin, S., Tzanakaki, G., Unemo, M., Vogel, U. and Zarantonelli, M. L. (2007) 'Target gene sequencing to characterize the penicillin G susceptibility of *Neisseria meningitidis*.' *Antimicrobial Agents and Chemotherapy*, 51(8) pp. 2784–2792.

Taha, M. K., Zarantonelli, M. L., Neri, A., Enriquez, R., Vázquez, J. A. and Stefanelli, P. (2006) 'Interlaboratory comparison of PCR-based methods for detection of penicillin G susceptibility in *Neisseria meningitidis*.' *Antimicrobial Agents and Chemotherapy*, 50(3) pp. 887–92.

Taha, M., Zarantonelli, M., Ruckly, C., Giorgini, D. and Michel Alonso, J. (2006) 'Rifampin-resistant *Neisseria meningitidis*.' *Emerging Infectious Diseases*, 12(5) pp. 859–860.

Tamura, K., Dudley, J., Nei, M. and Kumar, S. (2007) 'MEGA4: Molecular Evolutionary Genetics Analysis (MEGA) software version 4.0.' *Molecular biology and evolution*. United States, 24(8) pp. 1596–1599.

Terranella, A., Cohn, A. and Clark, T. (2011) 'Meningococcal conjugate vaccines: optimizing global impact.' *Infection and drug resistance*, 4 pp. 161–169.

Tettelin, H., Saunders, N. J., Heidelberg, J., Jeffries, A. C., Nelson, K. E., Eisen, J. A., Ketchum, K. A., Hood, D. W., Peden, J. F., Dodson, R. J., Nelson, W. C., Gwinn, M. L., DeBoy, R., Peterson, J. D., Hickey, E. K., Haft, D. H., Salzberg, S. L., White, O., Fleischmann, R. D., Dougherty, B. A., Mason, T., Ciecko, A., Parksey, D. S., Blair, E., Cittone, H., Clark, E. B., Cotton, M. D., Utterback, T. R., Khouri, H., Qin, H., Vamathevan, J., Gill, J., Scarlato, V., Masignani, V., Pizza, M., Grandi, G., Sun, L., Smith, H. O., Fraser, C. M., Moxon, E. R., Rappuoli, R. and Venter, J. C. (2000) 'Complete Genome Sequence of *Neisseria meningitidis* Serogroup B Strain MC58.' *Science*, 287(5459) pp. 1809–1815.

Thompson, M., Ninis, N., Perera, R., Mayon-White, R., Phillips, C., Bailey, L., Harnden, A., Mant, D. and Levin, M. (2006) 'Clinical recognition of meningococcal disease in children and adolescents.' *The Lancet*, 20(367) pp. 397–404.

Thulin, S., Olcén, P., Fredlund, H. and Unemo, M. (2006) 'Total variation in the penA gene

of *Neisseria meningitidis*: Correlation between susceptibility to β-lactam antibiotics and *penA* gene heterogeneity.' *Antimicrobial Agents and Chemotherapy*, 50(10) pp. 3317–3324.

Tomberg, J., Fedarovich, A., Vincent, L. R., Jerse, A. E., Unemo, M., Davies, C. and Nicholas, R. A. (2017) 'Alanine 501 mutations in penicillin-binding protein 2 from *Neisseria gonorrhoeae*: Structure, mechanism, and effects on cephalosporin resistance and biological fitness.' *Biochemistry*. American Chemical Society, 56(8) pp. 1140–1150.

Tomberg, J., Unemo, M., Davies, C. and Nicholas, R. A. (2010) 'Molecular and structural analysis of mosaic variants of penicillin-binding protein 2 conferring decreased susceptibility to expanded-spectrum cephalosporins in *Neisseria gonorrhoeae*: role of epistatic mutations.' *Biochemistry*, 49(37) pp. 8062–8070.

Toner, E., Adalja, A., Gronvall, G. K., Cicero, A. and Inglesby, T. V (2015) 'Antimicrobial resistance is a global health emergency.' *Health security*, 13(3) pp. 153–155.

Tsang, R. S. W., Ahmad, T., Jamieson, F. B. and Tyrrell, G. J. (2019) 'WGS analysis of a penicillin-resistant *Neisseria meningitidis* strain containing a chromosomal ROB-1 β-lactamase gene.' *Journal of Antimicrobial Chemotherapy*. Oxford University Press, 74(1) pp. 22–28.

Tsang, R. S. W., Ahmad, T., Tyler, S., Lefebvre, B., Deeks, S. L., Gilca, R., Hoang, L., Tyrrell, G., Van Caeseele, P., Van Domselaar, G. and Jamieson, F. B. (2018) 'Whole genome typing of the recently emerged Canadian serogroup W *Neisseria meningitidis* sequence type 11 clonal complex isolates associated with invasive meningococcal disease.' *International Journal of Infectious Diseases*, 69 pp. 55–62.

Tsang, R. S. W., Law, D. K. S., Deng, S. and Hoang, L. (2017) 'Ciprofloxacin-resistant *Neisseria meningitidis* in Canada: Likely imported strains.' *Canadian Journal of Microbiology*. Canadian Science Publishing pp. 265–268.

Tully, J., Viner, R. M., Coen, P. G., Stuart, J. M., Zambon, M., Peckham, C., Booth, C., Klein, N., Kaczmarski, E. and Booy, R. (2006) 'Risk and protective factors for meningococcal disease in adolescents: Matched cohort study.' *British Medical Journal*, 332(7539) pp. 445–448.

Turner, P. C., Southern, K. W., Spencer, N. J. and Pullen, H. (1990) 'Treatment failure in meningococcal meningitis.' *Lancet (London, England)*. England pp. 732–733.

Tzanakaki, G., Blackwell, C. C., Kremastinou, J., Kallergi, C., Kouppari, G. and Weir, D. M. (1992) 'Antibiotic sensitivities of *Neisseria meningitidis* isolates from patients and carriers in Greece.' *Epidemiology and infection*, 108(3) pp. 449–455.

Tzeng, Y.-L., Bazan, J. A., Turner, A. N., Wang, X., Retchless, A. C., Read, T. D., Toh, E., Nelson, D. E., Del Rio, C. and Stephens, D. S. (2017) 'Emergence of a new *Neisseria meningitidis* clonal complex 11 lineage 11.2 clade as an effective urogenital pathogen.' *Proceedings of the National Academy of Sciences of the United States of America*, 114(16) pp. 4237–4242.

Unemo, M. (2015) 'Current and future antimicrobial treatment of gonorrhoea - the rapidly evolving *Neisseria gonorrhoeae* continues to challenge.' *BMC infectious diseases*, 15, August, p. 364.

Unemo, M., Golparian, D., Nicholas, R., Ohnishi, M., Gallay, A. and Sednaoui, P. (2012) 'High-level cefixime- and ceftriaxone-resistant *Neisseria gonorrhoeae* in France: novel *penA* mosaic allele in a successful international clone causes treatment failure.' *Antimicrobial agents and chemotherapy*, 56(3) pp. 1273–1280.

Uriz, S., Pineda, V., Grau, M., Nava, J. M., Bella, F., Morera, M. A., Fontanals, D., Font, B., Martí, C. and Deulofeu, F. (1991) '*Neisseria meningitidis* with reduced sensitivity to penicillin: observations in 10 children.' *Scandinavian journal of infectious diseases*. England, 23(2) pp. 171–174.

Urwin, R. and Maiden, M. C. J. (2003) 'Multi-locus sequence typing: A tool for global epidemiology.' *Trends in Microbiology*, 11(10) pp. 479–487.

Vacca, I., Del Tordello, E., Gasperini, G., Pezzicoli, A., Di Fede, M., Rossi Paccani, S., Marchi, S., Mubaiwa, T. D., Hartley-Tassell, L. E., Jennings, M. P., Seib, K. L., Masignani, V., Pizza, M., Serruto, D., Aricò, B. and Delany, I. (2016) 'Neisserial heparin binding antigen (NHBA) contributes to the adhesion of *Neisseria meningitidis* to human epithelial cells.' *PloS one*, 11(10) pp. 1–17.

Vacca, P., Fazio, C., Neri, A., Ambrosio, L., Palmieri, A. and Stefanelli, P. (2018) '*Neisseria*

meningitidis antimicrobial resistance in Italy, 2006 to 2016.' *Antimicrobial Agents and Chemotherapy*, 62(9) pp. 1–6.

Vázquez, J. A. (2007) 'Resistance testing of meningococci: The recommendations of the European Monitoring Group on Meningococci.' *FEMS Microbiology Reviews*, 31(1) pp. 97–100.

Vázquez, J. A., Arreaza, L., Block, C., Ehrhard, I., Gray, S. J., Heuberger, S., Hoffmann, S., Kriz, P., Nicolas, P., Olcen, P., Skoczynska, A., Spanjaard, L., Stefanelli, P., Taha, M. K. and Tzanakaki, G. (2003) 'Interlaboratory comparison of agar dilution and Etest methods for determining the MICs of antibiotics used in management of *Neisseria meningitidis* infections.' *Antimicrobial Agents and Chemotherapy*, 47(11) pp. 3430–3434.

Vieusseux, G. (1805) 'Mιmoire sur la maladie qui a regnι a Genκve au printemps de 1805.' *Journal de Médecine, Chirurgie et Pharmacie*, 1 p. 163.

Villalba, M. de la C. M., Lay, L. de los A. R., Chandra, V., Corredor, M. B., Frometa, S. S., Moreno, A. G. and Jameel, S. (2008) 'Ciprofloxacin resistance in *Neisseria meningitidis* in France.' *Emerging Infectious Diseases*. Centers for Disease Control and Prevention (CDC), 14(8) pp. 1320–1322.

Virji, M., Makepeace, K., Ferguson, D. J., Achtman, M. and Moxon, E. R. (1993) 'Meningococcal Opa and Opc proteins: their role in colonization and invasion of human epithelial and endothelial cells.' *Molecular microbiology*. England, 10(3) pp. 499–510.

Wahdan, M. H., Rizk, F., el-Akkad, A. M., el-Ghoroury, A. A., Hablas, R., Girgis, N. I., Amer, A., Boctar, W., Sippel, J. E., Gotschlich, E. C., Triau, R., Sanborn, W. R. and Cvjetanovic, B. (1973) 'A controlled field trial of a serogroup A meningococcal polysaccharide vaccine.' *Bulletin of the World Health Organization*. Switzerland, 48(6) pp. 667–673.

Wedege, E. and Rosenqvist, E. (1990) 'Serotyping and subtyping of *Neisseria meningitidis* isolates by co-agglutination , dot-blotting and ELISA.' *Medical Microbiology*, 31(May 1989) pp. 195–201.

Wehrli, W. (1983) 'Rifampin: mechanisms of action and resistance.' *Reviews of infectious diseases*. United States, 5(3) pp. S407-11.

Weidlich, L., Baethgen, L. F., Mayer, L. W., Moraes, C., Klein, C. C., Nunes, L. S., Rios, S. da S., Kmetzsch, C. I., Rossetti, M. L. R. and Zaha, A. (2008) 'High prevalence of *Neisseria meningitidis* hypervirulent lineages and emergence of W135:P1.5,2:ST-11 clone in Southern Brazil.' *Journal of Infection*, 57(4) pp. 324–331.

Whiley, D. M., Goire, N., Lambert, S. B., Ray, S., Limnios, E. A., Nissen, M. D., Sloots, T. P. and Tapsall, J. W. (2010) 'Reduced susceptibility to ceftriaxone in *Neisseria gonorrhoeae* is associated with mutations G542S, P551S and P551L in the gonococcal penicillin-binding protein 2.' *The Journal of antimicrobial chemotherapy*. England, 65(8) pp. 1615–1618.

Whiley, D. M., Limnios, E. A., Ray, S., Sloots, T. P. and Tapsall, J. W. (2007) 'Diversity of *penA* alterations and subtypes in *Neisseria gonorrhoeae* strains from Sydney, Australia, that are less susceptible to ceftriaxone.' *Antimicrobial agents and chemotherapy*, 51(9) pp. 3111–3116.

Wilder-Smith, A., Barkham, T. M. S., Ravindran, S., Earnest, A. and Paton, N. I. (2003) 'Persistance of W135 *Neisseria meningitidis* carriage in returning Hajj pilgrims: Risk for early and late transmission to household contacts.' *Emerging Infectious Diseases*, 9(1) pp. 123–126.

Wilder-Smith, A., Goh, K. T., Barkham, T. and Paton, N. I. (2003) 'Hajj-associated outbreak strain of *Neisseria meningitidis* serogroup W135: estimates of the attack rate in a defined population and the risk of invasive disease developing in carriers.' *Clinical Infectious Diseases*, 36(6) pp. 679–683.

Willerton, L., Lucidarme, J., Campbell, H., Caugant, D. A., Claus, H., Jacobsson, S., Ladhani, S. N., Mölling, P., Neri, A., Stefanelli, P., Taha, M. K., Vogel, U. and Borrow, R. (2020) 'Geographically widespread invasive meningococcal disease caused by a ciprofloxacin resistant non-groupable strain of the ST-175 clonal complex.' *Journal of Infection*. Elsevier Ltd, 81(4) pp. 575–584.

Williamson, R., Collatz, E. and Gutmann, L. (1986) 'Mechanisms of action of beta-lactam antibiotics and mechanisms of non-enzymatic resistance.' *Presse medicale (Paris, France : 1983)*. France, 15(46) pp. 2282–2289.

Wise, J. (1999) 'UK introduces new meningitis C vaccine.' *BMJ (Clinical research ed.)* p.

278.

Woodford, N. and Ellington, M. J. (2007) 'The emergence of antibiotic resistance by mutation.' *Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases*. England, 13(1) pp. 5–18.

Woods, C. R., Smith, A. L., Wasilauskas, B. L., Campos, J. and Givner, L. B. (1994) 'Invasive disease caused by *Neisseria meningitidis* relatively resistant to penicillin in North Carolina.' *The Journal of infectious diseases*. United States, 170(2) pp. 453–456.

World Health Organization (2011) *Laboratory methods for the diagnosis of meningitis caused by Neisseria meningitidis, Streptococcus pneumoniae and Haemophilus influenzae*. Centers for Disease Control and Prevention. [Online] [Accessed on 26th March 2021] https://www.cdc.gov/meningitis/lab-manual/index.html.

World Health Organization (2014) *Antimicrobial resistance: Global report on surveillance*. [Online] [Accessed on 26th March 2021] https://www.who.int/antimicrobial-resistance/publications/surveillancereport/en/.

World Health Organization (2020) *Defeating meningitis by 2030 : a global road map*. Available online at https://www.who.int/publications/m/item/defeating-meningitis-by-2030-a-global-road-map). [Online] [Accessed on 26th March 2021] https://www.who.int/initiatives/defeating-meningitis-by-2030.

World Health Organization (WHO) (2001) 'Meningococcal disease, serogroup W135 (update).' *Weekly epidemiological record; Health Section of the Secretariat of the League of Nations*, 76(28) pp. 213–214.

Wu, H. M., Harcourt, B. H., Hatcher, C. P., Wei, S. C., Novak, R. T., Wang, X., Juni, B. A., Glennen, A., Boxrud, D. J., Rainbow, J., Schmink, S., Mair, R. D., Theodore, M. J., Sander, M. A., Miller, T. K., Kruger, K., Cohn, A. C., Clark, T. A., Messonnier, N. E., Mayer, L. W. and Lynfield, R. (2009) 'Emergence of ciprofloxacin-resistant *Neisseria meningitidis* in North America.' *The New England journal of medicine*. United States, 360(9) pp. 886–892.

Xu, Z., Zhu, B., Xu, L., Gao, Y. and Shao, Z. (2015) 'First case of *Neisseria meningitidis* capsule null locus infection in China.' *Infectious Diseases*, 47(8) pp. 591–592.

Yazdankhah, S. P. and Caugant, D. A. (2004) '*Neisseria meningitidis*: An overview of the carriage state.' *Journal of Medical Microbiology*, 53(9) pp. 821–832.

Yezli, S. (2018) 'The threat of meningococcal disease during the Hajj and Umrah mass gatherings: A comprehensive review.' *Travel Medicine and Infectious Disease*. Elsevier USA pp. 51–58.

Yezli, S., Assiri, A. M., Alhakeem, R. F., Turkistani, A. M. and Alotaibi, B. (2016) 'Meningococcal disease during the Hajj and Umrah mass gatherings.' *International Journal of Infectious Diseases*, 47 pp. 60–64.

Yezli, S., Bin Saeed, A. A., Assiri, A. M., Alhakeem, R. F., Yunus, M. A., Turkistani, A. M., Booy, R. and Alotaibi, B. M. (2016) 'Prevention of meningococcal disease during the Hajj and Umrah mass gatherings: Past and current measures and future prospects.' *International Journal of Infectious Diseases*. International Society for Infectious Diseases, 47 pp. 71–78.

Zapun, A., Morlot, C. and Taha, M.-K. (2016) 'Resistance to β-lactams in *Neisseria* spp due to chromosomally encoded penicillin-binding proteins.' *Antibiotics*. MDPI AG, 5(4) p. 35.

Zhao, S., Duncan, M., Tomberg, J., Davies, C., Unemo, M. and Nicholas, R. A. (2009) 'Genetics of chromosomally mediated intermediate resistance to ceftriaxone and cefixime in *Neisseria gonorrhoeae*.' *Antimicrobial Agents and Chemotherapy*, 53(9) pp. 3744–3751.

Zhu, B., Fan, Y., Xu, Z., Xu, L., Du, P., Gao, Y. and Shao, Z. (2014) 'Genetic diversity and clonal characteristics of ciprofloxacin-resistant meningococcal strains in China.' *Journal of Medical Microbiology*. Microbiology Society, 63, November, pp. 1411–1418.

Zhu, B., Xu, Z., Du, P., Xu, L., Sun, X., Gao, Y. and Shao, Z. (2015) 'Sequence type 4821 clonal complex serogroup B *Neisseria meningitidis* in China, 1978-2013.' *Emerging infectious diseases*, 21(6) pp. 925–932.

Zumla, A. and Memish, Z. A. (2019) 'Risk of antibiotic resistant meningococcal infections in Hajj pilgrims.' *The BMJ*, 366(August) pp. 1–2.

Zunt, J. R., Kassebaum, N. J., Blake, N. and Collaborators, G. 2016 M. (2018) 'Global,

regional, and national burden of meningitis, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016.' *The Lancet Neurology*, 17(12) pp. 1061–1082.

6 Appendices

Appendix 1: Isolate panel 1; Results chapters 3.1 and 3.3.

PubMLST ID	Country	Epi Year	Serogroup	Genogroup	ST	CC	Site	Penicillin MIC (mg/L)	Rifampicin MIC (mg/L)	Ciprofloxicin MIC (mg/L)	Cefotaxime MIC (mg/L)
18968	England	2010/11	B	B	269	ST-269 complex	CSF	0.047	0.008	0.004	0.002
18969	England	2010/11	B	B	1194	ST-41/44 complex	Blood	0.064	0.008	0.004	0.003
19023	England	2010/11	B	B	1161	ST-269 complex	Blood	0.064	0.008	0.004	0.004
19024	England	2010/11	B	B	1194	ST-41/44 complex	Blood	0.19	0.006	0.003	0.003
19025	England	2010/11	B	B	1831	UA	Blood	0.064	0.004	0.004	0.004
19026	England	2010/11	B	B	3754	ST-41/44 complex	Blood	0.047	0.008	0.004	0.002
19027	England	2010/11	B	B	1097	ST-41/44 complex	Blood	0.047	0.008	0.004	0.004
19028	England	2010/11	B	B	275	ST-269 complex	Blood	0.047	0.023	0.004	0.003
19029	England	2010/11	B	B	1049	ST-269 complex	Blood	0.064	0.002	0.006	0.004
19030	England	2010/11	B	B	461	ST-461 complex	Blood	0.19	0.016	0.004	0.003
19031	England	2010/11	B	B	1161	ST-269 complex	Blood	0.094	0.016	0.006	0.006
19032	Wales	2010/11	B	B	41	ST-41/44 complex	Blood	0.047	0.004	0.004	0.002
19958	England	2010/11	B	B	9812	ST-213 complex	Blood	0.047	0.006	0.003	0.003
19959	England	2010/11	B	B	275	ST-269 complex	Blood	0.047	0.006	0.004	0.003
19960	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.047	0.032	0.006	0.003
19961	England	2010/11	B	B	340	ST-41/44 complex	Blood	0.047	0.008	0.004	0.003
19962	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.064	0.008	0.003	0.004
19963	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.004
19964	England	2010/11	Y	Y	183	ST-23 complex	Blood	0.38	0.006	0.004	0.006
19965	England	2010/11	B	B	1575	UA	Blood	0.023	0.006	0.004	0.002
19966	England	2010/11	B	B	4713	UA	Blood	0.064	0.006	0.004	0.006
19967	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.125	0.004	0.004	0.003
19969	England	2010/11	B	B	269	ST-269 complex	Blood	0.032	0.006	0.004	0.002
19970	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.006
19971	England	2010/11	B	B	3802	ST-41/44 complex	Blood	0.094	0.016	0.004	0.003
19972	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.064	0.004	0.003	0.003
19973	England	2010/11	B	B	2931	ST-32 complex	Blood	0.125	0.023	0.004	0.008
19974	England	2010/11	B	B	269	ST-269 complex	Blood	0.047	0.008	0.006	<0.002
19975	England	2010/11	B	B	7833	ST-269 complex	Blood	0.064	0.004	0.006	0.004
19976	England	2010/11	Y	Y	9813	ST-23 complex	Blood	0.064	0.006	0.004	0.004
19977	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.006
19978	England	2010/11	B	B	41	ST-41/44 complex	CSF	0.047	0.016	0.004	0.003
19979	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.006
19980	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.006
19981	England	2010/11	Y	Y	9814	ST-23 complex	Blood	0.047	0.004	0.004	0.003
19983	England	2010/11	B	B	749	ST-32 complex	Blood	0.19	0.008	0.003	0.004
19984	England	2010/11	B	B	340	ST-41/44 complex	Blood	0.047	0.006	0.006	0.003
19985	Wales	2010/11	B	B	41	ST-41/44 complex	Blood	0.047	0.008	0.004	0.003
19986	England	2010/11	B	B	1163	ST-269 complex	Blood	0.25	0.006	0.006	0.004
19987	Wales	2010/11	B	B	1161	ST-269 complex	Blood	0.125	0.008	0.004	0.008
19988	England	2010/11	B	B	9815	ST-41/44 complex	CSF	0.047	0.016	0.004	0.004
19989	Wales	2010/11	B	B	1992	ST-41/44 complex	CSF	0.19	0.008	0.004	0.003
19990	Wales	2010/11	B	B	162	ST-162 complex	Blood	0.25	0.064	0.004	0.006
19991	England	2010/11	B	B	213	ST-213 complex	Blood	0.047	0.032	0.003	0.003
19992	England	2010/11	B	B	213	ST-213 complex	Blood	0.064	0.008	0.004	0.004
19993	England	2010/11	B	B	18	ST-18 complex	Blood	0.047	0.016	0.003	0.004
19994	England	2010/11	B	B	5357	ST-41/44 complex	Blood	0.047	0.004	0.004	0.002
19996	England	2010/11	B	B	34	ST-32 complex	Blood	0.064	0.094	0.004	0.006
19997	England	2010/11	B	B	3687	UA	Blood	0.047	0.023	0.004	0.003
19998	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.003
19999	Northern Ireland	2010/11	NG	CNL	1136	ST-1136 complex	Blood	0.19	0.032	0.006	0.006
20000	England	2010/11	B	B	34	ST-32 complex	Blood	0.064	0.016	0.004	0.004
20001	England	2010/11	B	B	9816	UA	CSF	0.047	0.023	0.004	0.004
20002	England	2010/11	B	B	46	ST-41/44 complex	Blood	0.047	0.012	0.004	0.003
20003	England	2010/11	B	B	485	ST-41/44 complex	Blood	0.19	0.006	0.004	0.004
20004	England	2010/11	B	B	9879	ST-41/44 complex	CSF	0.047	0.012	0.004	0.004
20005	England	2010/11	B	B	40	ST-41/44 complex	Blood	0.125	0.047	0.003	0.004
20006	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.047	0.006	0.003	0.003
20007	England	2010/11	B	B	461	ST-461 complex	Blood	0.064	0.032	0.003	0.004
20008	England	2010/11	B	B	6782	ST-41/44 complex	Blood	0.032	0.023	0.003	0.004
20009	England	2010/11	B	B	213	ST-213 complex	CSF	0.047	0.016	0.004	0.004
20010	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.032	0.016	0.003	0.002
20011	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.064	0.012	0.006	0.003
20012	England	2010/11	B	B	1161	ST-269 complex	Blood	0.064	0.016	0.004	0.004
20013	Northern Ireland	2010/11	B	B	8384	ST-41/44 complex	Blood	0.032	0.012	0.004	0.003
20014	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.032	0.012	0.003	0.003
20015	England	2010/11	B	B	213	ST-213 complex	Blood	0.016	0.047	0.003	0.003
20016	England	2010/11	C	C	5133	ST-103 complex	Blood	0.008	0.064	0.003	<0.002
20017	England	2010/11	B	B	749	ST-32 complex	Blood	0.125	0.012	0.004	0.008
20018	England	2010/11	B	B	269	ST-269 complex	Blood	0.047	0.006	0.006	0.003
20019	England	2010/11	B	B	1161	ST-269 complex	CSF	0.064	0.012	0.006	0.004
20020	England	2010/11	B	B	9817	UA	Blood	0.064	0.094	0.003	0.006
20021	England	2010/11	W	W	1224	ST-22 complex	Blood	0.094	0.016	0.004	0.003
20022	England	2010/11	B	B	213	ST-213 complex	Blood	0.19	0.032	0.003	0.004
20023	England	2010/11	E	E	2435	ST-60 complex	Blood	0.25	0.032	0.003	0.006
20024	England	2010/11	B	B	213	ST-213 complex	Blood	0.032	0.016	0.004	0.003
20025	Wales	2010/11	B	B	213	ST-213 complex	CSF	0.064	0.047	0.003	0.003
20026	England	2010/11	B	B	9880	UA	Blood	0.023	0.012	0.004	0.004
20027	England	2010/11	B	B	1161	ST-269 complex	Blood	0.064	0.012	0.004	0.003
20028	England	2010/11	B	B	275	ST-269 complex	Blood	0.047	0.006	0.003	0.003
20029	England	2010/11	B	B	4401	ST-269 complex	Blood	0.19	0.004	0.004	0.004
20030	England	2010/11	B	B	6083	ST-32 complex	Blood	0.047	0.047	0.004	0.003
20031	England	2010/11	C	C	467	ST-269 complex	Joint	0.047	0.032	0.004	0.003

20032	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.032	0.006	0.003	0.003
20034	Northern Ireland	2010/11	B	B	42	ST-41/44 complex	Blood	0.047	0.012	0.006	0.002
20035	England	2010/11	B	B	1157	ST-1157 complex	CSF	0.094	0.064	0.004	0.006
20036	England	2010/11	B	B	275	ST-269 complex	Blood	0.047	0.016	0.004	0.003
20037	England	2010/11	B	B	284	UA	Blood	0.032	0.012	0.004	<0.002
20038	England	2010/11	B	B	1831	UA	Blood	0.064	0.012	0.004	0.004
20039	England	2010/11	W	W	184	ST-22 complex	Blood	0.125	0.016	0.006	0.003
20040	England	2010/11	B	B	5335	UA	Blood	0.023	0.006	0.004	<0.002
20041	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.047	0.004	0.004	0.004
20042	England	2010/11	Y	Y	3651	ST-22 complex	Blood	0.094	0.023	0.008	0.008
20043	England	2010/11	B	B	283	ST-269 complex	Blood	0.047	0.006	0.004	0.003
20044	England	2010/11	B	B	275	ST-269 complex	Blood	0.064	0.008	0.004	0.003
20045	England	2010/11	B	B	2123	UA	Blood	0.023	0.023	0.004	0.002
20046	England	2010/11	B	B	9881	ST-213 complex	Blood	0.047	0.016	0.004	0.004
20047	England	2010/11	B	B	275	ST-269 complex	Blood	0.19	0.008	0.006	0.008
20048	England	2010/11	B	B	35	ST-35 complex	Blood	0.047	0.125	0.004	0.003
20049	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.064	0.032	0.006	0.003
20050	England	2010/11	B	B	1161	ST-269 complex	Blood	0.125	0.006	0.004	0.004
20051	England	2010/11	B	B	9882	ST-41/44 complex	Blood	0.125	0.006	0.006	0.004
20052	England	2010/11	B	B	213	ST-213 complex	Blood	0.047	0.016	0.004	0.003
20053	England	2010/11	W/Y	W/Y	1466	ST-174 complex	Blood	0.125	0.032	0.003	0.006
20054	England	2010/11	X	X	9839	UA	Blood	0.19	0.012	0.006	0.004
20055	England	2010/11	B	B	1992	ST-41/44 complex	CSF	0.047	0.004	0.006	0.003
20056	England	2010/11	B	B	269	ST-269 complex	Blood	0.032	0.006	0.006	0.002
20058	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.125	0.006	0.004	0.004
20059	England	2010/11	Y	Y	168	ST-167 complex	Blood	0.047	0.006	0.006	0.004
20060	England	2010/11	B	B	9828	UA	CSF	0.047	0.032	0.006	0.002
20061	England	2010/11	B	B	1575	UA	Blood	0.094	0.032	0.004	0.003
20062	England	2010/11	B	B	340	ST-41/44 complex	Blood	0.125	0.008	0.004	0.003
20063	England	2010/11	B	B	9883	ST-41/44 complex	Blood	0.047	0.004	0.003	0.003
20064	Northern Ireland	2010/11	B	B	269	ST-269 complex	Blood	0.032	0.032	0.006	0.003
20065	Wales	2010/11	B	B	18	ST-18 complex	Blood	0.032	0.016	0.004	<0.002
20066	England	2010/11	B	B	11	ST-11 complex	Blood	0.047	0.064	0.004	0.003
20067	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.032	0.006	0.003	0.003
20068	England	2010/11	B	B	60	ST-60 complex	Blood	0.064	0.125	0.006	0.004
20069	England	2010/11	B	B	154	ST-41/44 complex	Blood	0.023	0.003	0.003	<0.002
20070	Wales	2010/11	B	B	1090	ST-41/44 complex	Blood	0.125	0.004	0.003	0.002
20071	England	2010/11	B	B	1430	ST-60 complex	Blood	0.064	0.016	0.004	0.004
20072	England	2010/11	Y	Y	1466	ST-174 complex	Blood	0.094	0.008	0.003	0.003
20073	England	2010/11	B	B	282	ST-282 complex	Blood	0.032	0.008	0.006	0.002
20074	England	2010/11	Y	Y	6463	ST-23 complex	Blood	0.047	0.006	0.004	0.003
20075	England	2010/11	B	B	213	ST-213 complex	Blood	0.047	0.006	0.003	0.003
20076	England	2010/11	B	B	154	ST-41/44 complex	Blood	0.047	0.016	0.004	0.003
20077	England	2010/11	B	B	9884	ST-213 complex	Blood	0.064	0.012	0.006	0.004
20078	England	2010/11	B	B	269	ST-269 complex	Blood	0.032	0.006	0.006	0.002
20079	England	2010/11	C	C	5133	ST-103 complex	CSF	0.016	0.002	0.004	<0.002
20080	England	2010/11	B	B	1194	ST-41/44 complex	Blood	0.19	0.008	0.004	0.004
20081	England	2010/11	B	B	1195	ST-269 complex	Blood	0.047	0.006	0.006	0.003
20082	England	2010/11	B	B	479	ST-269 complex	Blood	0.047	0.006	0.006	0.002
20083	England	2010/11	B	B	275	ST-269 complex	Blood	0.094	0.004	0.006	0.004
20084	England	2010/11	B	B	213	ST-213 complex	Blood	0.023	0.004	0.004	0.003
20085	England	2010/11	B	B	9829	ST-269 complex	Blood	0.032	0.006	0.004	<0.002
20086	England	2010/11	B	B	461	ST-461 complex	CSF	0.094	0.047	0.003	0.004
20087	England	2010/11	B	B	9830	ST-213 complex	Blood	0.047	0.016	0.006	0.003
20088	England	2010/11	B	B	9885	ST-60 complex	Blood	0.19	0.012	0.004	0.004
20089	England	2010/11	B	B	34	ST-32 complex	Blood	0.125	0.008	0.004	0.008
20090	England	2010/11	B	B	479	ST-269 complex	Blood	0.032	0.012	0.004	0.002
20091	England	2010/11	B	B	318	ST-41/44 complex	Blood	0.064	0.008	0.006	0.004
20092	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.25	0.008	0.006	0.004
20093	Wales	2010/11	B	B	41	ST-41/44 complex	Blood	0.032	0.006	0.006	0.003
20094	England	2010/11	B	B	1194	ST-41/44 complex	Blood	0.047	0.006	0.006	0.002
20095	England	2010/11	B	B	9840	ST-269 complex	Blood	0.064	0.004	0.006	0.004
20096	England	2010/11	B	B	1049	ST-269 complex	Blood	0.047	0.016	0.008	0.003
20097	England	2010/11	B	B	9886	ST-41/44 complex	CSF	0.047	0.008	0.006	0.003
20098	England	2010/11	B	B	9887	UA	Blood	0.047	0.012	0.004	0.004
20099	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.064	0.004	0.008	0.008
20100	England	2010/11	B	B	3934	UA	Blood	0.064	0.004	0.004	0.004
20101	England	2010/11	W	W	1281	ST-22 complex	Blood	0.125	0.006	0.006	0.003
20102	England	2010/11	B	B	8955	ST-213 complex	Blood	0.064	0.012	0.004	0.004
20103	England	2010/11	B	B	269	ST-269 complex	Blood	0.125	0.016	0.006	0.006
20105	England	2010/11	B	B	9841	ST-41/44 complex	Blood	0.19	0.008	0.006	0.004
20106	England	2010/11	B	B	1097	ST-41/44 complex	Blood	0.064	0.004	0.004	0.003
20107	England	2010/11	B	B	485	ST-41/44 complex	Blood	0.25	0.006	0.006	0.004
20108	England	2010/11	B	B	485	ST-41/44 complex	Blood	0.19	0.006	0.008	0.004
20109	England	2010/11	B	B	8203	ST-41/44 complex	Blood	0.047	0.008	0.006	0.003
20110	England	2010/11	B	B	213	ST-213 complex	CSF	0.125	0.004	0.004	0.003
20111	England	2010/11	B	B	1161	ST-269 complex	Blood	0.064	0.008	0.006	0.006
20112	England	2010/11	B	B	34	ST-32 complex	Blood	0.047	0.032	0.006	0.004
20113	England	2010/11	B	B	46	ST-41/44 complex	Blood	0.047	0.006	0.008	0.002
20114	England	2010/11	W	W	2114	ST-22 complex	Blood	0.064	0.006	0.006	0.004
20115	England	2010/11	Y	Y	1466	ST-174 complex	Blood	0.094	0.032	0.003	0.004
20116	England	2010/11	B	B	1938	ST-41/44 complex	Blood	0.032	0.003	0.002	0.002
20117	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.004	0.003
20118	England	2010/11	B	B	4051	UA	Blood	0.032	0.016	0.003	0.003
20119	England	2010/11	B	B	479	ST-269 complex	Blood	0.047	0.008	0.006	0.003

20120	Wales	2010/11	B	B	34	ST-32 complex	Blood	0.047	0.012	0.006	0.003
20121	England	2010/11	B	B	2873	ST-269 complex	Blood	0.064	0.008	0.006	0.003
20122	England	2010/11	B	B	1195	ST-269 complex	CSF	0.047	0.008	0.006	0.002
20123	England	2010/11	B	B	8068	ST-282 complex	CSF	0.064	0.023	0.006	0.004
20124	England	2010/11	B	B	1161	ST-269 complex	Blood	0.094	0.008	0.004	0.004
20125	England	2010/11	B	B	9841	ST-41/44 complex	Joint	0.19	0.008	0.004	0.006
20126	Wales	2010/11	B	B	1161	ST-269 complex	Blood	0.094	0.008	0.006	0.004
20127	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.25	0.008	0.006	0.006
20128	England	2010/11	Y	Y	1655	ST-23 complex	CSF	0.047	0.004	0.004	0.004
20129	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.047	0.004	0.003	0.002
20130	Wales	2010/11	B	B	9187	ST-213 complex	Blood	0.094	0.016	0.004	0.004
20131	England	2010/11	B	B	269	ST-269 complex	Blood	0.032	0.006	0.006	0.003
20132	England	2010/11	Y	Y	3651	ST-22 complex	Blood	0.064	0.016	0.006	0.004
20133	England	2010/11	B	B	1161	ST-269 complex	Blood	0.094	0.032	0.004	0.004
20134	England	2010/11	B	B	3447	ST-41/44 complex	Blood	0.047	0.008	0.006	0.003
20135	England	2010/11	Y	Y	9831	ST-23 complex	Blood	0.064	0.004	0.006	0.004
20136	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.003
20137	Wales	2010/11	B	B	5981	ST-41/44 complex	Blood	0.047	0.006	0.006	0.003
20138	Wales	2010/11	B	B	283	ST-269 complex	Blood	0.064	0.016	0.006	0.003
20139	England	2010/11	B	B	259	ST-32 complex	Blood	0.064	0.008	0.006	0.006
20140	England	2010/11	B	B	6782	ST-41/44 complex	Blood	0.125	0.023	0.004	0.004
20141	England	2010/11	B	B	32	ST-32 complex	Blood	0.19	0.008	0.004	0.004
20142	England	2010/11	B	B	136	ST-41/44 complex	Blood	0.032	0.064	0.004	0.003
20143	England	2010/11	Y	Y	1655	ST-23 complex	Joint	0.047	0.004	0.004	0.003
20144	England	2010/11	B	B	213	ST-213 complex	Blood	0.064	0.016	0.004	0.004
20145	England	2010/11	B	B	1194	ST-41/44 complex	Blood	0.38	0.006	0.006	0.004
20146	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.003	0.004
20147	England	2010/11	B	B	4713	UA	Blood	0.064	0.008	0.004	0.004
20148	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.19	0.006	0.004	0.004
20149	England	2010/11	B	B	1092	ST-269 complex	Blood	0.19	0.006	0.003	0.008
20150	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.047	0.012	0.004	0.003
20151	England	2010/11	B	B	162	ST-162 complex	Blood	0.064	0.047	0.003	0.003
20152	England	2010/11	B	B	9888	ST-1157 complex	Blood	0.032	0.004	0.003	0.002
20153	Wales	2010/11	B	B	1161	ST-269 complex	Blood	0.064	0.008	0.003	0.004
20155	England	2010/11	C	C	11	ST-11 complex	Blood	0.064	0.047	0.004	0.004
20156	England	2010/11	B	B	1163	ST-269 complex	Blood	0.064	0.006	0.004	0.003
20157	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.032	0.004	0.003	0.003
20159	England	2010/11	W	W	1224	ST-22 complex	Blood	0.19	0.008	0.004	0.004
20160	England	2010/11	B	B	1097	ST-41/44 complex	Blood	0.064	0.003	0.004	0.003
20161	England	2010/11	B	B	32	ST-32 complex	Blood	0.047	0.004	0.004	0.004
20162	England	2010/11	B	B	9818	ST-60 complex	CSF	0.047	0.004	0.004	0.003
20163	England	2010/11	B	B	7789	ST-269 complex	CSF	0.064	0.006	0.004	0.004
20164	England	2010/11	Y	Y	23	ST-23 complex	Joint	0.25	0.004	0.004	0.008
20165	England	2010/11	B	B	1946	ST-461 complex	Blood	0.38	0.006	0.004	0.006
20166	England	2010/11	B	B	4954	UA	Blood	0.25	0.008	0.004	0.008
20167	England	2010/11	B	B	9889	ST-41/44 complex	Blood	0.19	0.008	0.003	0.006
20168	Wales	2010/11	B	B	1161	ST-269 complex	Blood	0.094	0.006	0.004	0.004
20169	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.064	<0.002	0.003	0.003
20170	Wales	2010/11	B	B	8049	ST-32 complex	Blood	0.19	0.003	0.003	0.003
20171	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.003	0.004
20172	England	2010/11	B	B	2783	ST-41/44 complex	Blood	0.032	0.008	0.003	0.002
20173	England	2010/11	B	B	269	ST-269 complex	Blood	0.047	0.004	0.004	0.003
20174	England	2010/11	B	B	42	ST-41/44 complex	Blood	0.012	<0.002	0.003	<0.002
20175	England	2010/11	B	B	154	ST-41/44 complex	Blood	0.047	0.003	0.003	0.003
20176	England	2010/11	B	B	9890	ST-32 complex	CSF	0.047	0.032	0.004	0.004
20177	England	2010/11	B	B	9891	ST-461 complex	Blood	0.023	0.012	0.003	<0.002
20178	England	2010/11	B	B	1159	UA	Blood	0.047	0.004	0.003	0.003
20179	Wales	2010/11	B	B	1096	ST-32 complex	CSF	0.047	0.006	0.003	0.003
20180	Northern Ireland	2010/11	B	B	9819	ST-41/44 complex	Blood	0.032	0.006	0.004	0.004
20181	England	2010/11	B	B	9820	ST-41/44 complex	Blood	0.064	0.008	0.003	0.006
20182	England	2010/11	B	B	8063	ST-35 complex	Blood	0.125	0.012	0.003	0.004
20183	England	2010/11	B	B	259	ST-32 complex	Blood	0.094	0.012	0.003	0.006
20184	Wales	2010/11	B	B	1161	ST-269 complex	Blood	0.064	0.016	0.004	0.004
20185	Wales	2010/11	B	B	41	ST-41/44 complex	Blood	0.047	0.004	0.002	0.003
20186	Wales	2010/11	B	B	1097	ST-41/44 complex	Blood	0.047	0.008	0.004	0.003
20187	England	2010/11	B	B	1049	ST-269 complex	Blood	0.047	0.003	0.003	0.003
20188	England	2010/11	B	B	1049	ST-269 complex	Blood	0.064	0.008	0.004	0.003
20189	England	2010/11	B	B	60	ST-60 complex	Blood	0.047	0.004	0.003	0.002
20190	England	2010/11	B	B	60	ST-60 complex	Blood	0.032	0.004	0.002	0.003
20191	England	2010/11	W	W	1286	ST-22 complex	Blood	0.094	0.004	0.003	0.002
20192	England	2010/11	B	B	269	ST-269 complex	Blood	0.047	0.004	0.004	0.003
20193	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.003	0.004
20194	England	2010/11	B	B	5849	UA	Blood	0.094	0.016	0.002	0.004
20195	England	2010/11	B	B	5861	ST-41/44 complex	CSF	0.094	0.006	0.002	0.003
20196	Wales	2010/11	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.004
20197	Wales	2010/11	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.003	0.004
20198	England	2010/11	B	B	34	ST-32 complex	Blood	0.19	0.004	0.004	0.008
20199	England	2010/11	Y	Y	168	ST-167 complex	Blood	0.047	0.008	0.003	0.002
20200	Wales	2010/11	B	B	1802	ST-282 complex	Blood	0.047	0.004	0.004	0.003
20201	England	2010/11	B	B	1196	ST-41/44 complex	Blood	0.047	0.004	0.003	0.003
20202	England	2010/11	B	B	477	ST-41/44 complex	Blood	0.064	0.094	0.004	0.008
20203	England	2010/11	B	B	1946	ST-461 complex	Blood	0.19	0.006	0.003	0.004
20204	England	2010/11	Y	Y	9842	ST-23 complex	Blood	0.094	0.008	0.004	0.008
20205	Wales	2010/11	B	B	9843	ST-269 complex	Blood	0.032	0.006	0.002	0.003
20206	England	2010/11	B	B	858	ST-18 complex	Blood	0.047	0.003	0.003	0.002

20207	England	2010/11	B	B	213	ST-213 complex	Blood	0.047	0.012	0.003	0.004
20208	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.003	0.003
20209	England	2010/11	B	B	60	ST-60 complex	Blood	0.064	0.004	0.003	0.004
20210	England	2010/11	B	B	213	ST-213 complex	CSF	0.064	0.008	0.003	0.004
20211	Wales	2010/11	B	B	461	ST-461 complex	Blood	0.19	0.006	0.003	0.006
20212	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.064	0.006	0.004	0.003
20213	Wales	2010/11	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.004	0.002
20214	Wales	2010/11	B	B	41	ST-41/44 complex	Blood	0.047	0.004	0.003	0.003
20215	England	2010/11	B	B	11	ST-11 complex	Blood	0.064	0.016	0.003	0.004
20217	England	2010/11	B	B	275	ST-269 complex	Blood	0.19	0.008	0.004	0.006
20218	England	2010/11	B	B	9832	ST-41/44 complex	Blood	0.047	0.006	0.003	0.003
20219	England	2010/11	B	B	2380	ST-35 complex	Blood	0.064	0.004	0.003	0.003
20220	England	2010/11	B	B	9833	ST-213 complex	Blood	0.047	0.016	0.002	0.003
20222	England	2010/11	B	B	41	ST-41/44 complex	CSF	0.19	0.008	0.004	0.006
20223	England	2010/11	Y	Y	7786	UA	Blood	0.064	0.012	0.003	0.006
20224	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.006
20225	England	2010/11	B	B	275	ST-269 complex	Blood	0.047	0.002	0.004	0.004
20227	England	2010/11	NG	Y	9844	UA	Blood	0.094	0.023	0.004	0.006
20228	England	2010/11	B	B	35	ST-35 complex	Blood	0.047	0.006	0.004	0.003
20229	England	2010/11	B	B	269	ST-269 complex	Blood	0.047	0.016	0.003	0.003
20230	England	2010/11	Y	Y	767	ST-167 complex	Blood	0.064	0.002	0.004	0.004
20231	England	2010/11	B	B	275	ST-269 complex	Blood	0.064	0.004	0.003	0.003
20232	England	2010/11	Y	Y	1466	ST-174 complex	Blood	0.125	0.016	0.002	0.006
20233	Wales	2010/11	B	B	213	ST-213 complex	CSF	0.125	0.023	0.004	0.008
20234	England	2010/11	C	C	11	ST-11 complex	Blood	0.064	0.016	0.004	0.004
20235	England	2010/11	B	B	269	ST-269 complex	Blood	0.047	0.004	0.003	0.002
20236	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.003	0.003
20237	England	2010/11	B	B	1194	ST-41/44 complex	Blood	0.047	0.004	0.004	0.003
20238	England	2010/11	B	B	290	ST-32 complex	Blood	0.064	0.006	0.003	0.002
20239	England	2010/11	B	B	461	ST-461 complex	Blood	0.125	0.006	0.003	0.004
20240	Wales	2010/11	B	B	4997	ST-18 complex	Blood	0.25	0.016	0.004	0.008
20241	England	2010/11	B	B	340	ST-41/44 complex	Blood	0.064	0.008	0.004	0.003
20242	England	2010/11	B	B	1774	ST-269 complex	Blood	0.064	0.006	0.004	0.002
20243	England	2010/11	B	B	485	ST-41/44 complex	Blood	0.19	0.064	0.004	0.003
20244	Wales	2010/11	C	C	5133	ST-103 complex	Blood	0.016	0.002	0.002	<0.002
20245	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.003	0.002
20246	England	2010/11	B	B	2799	ST-41/44 complex	Blood	0.047	0.003	0.003	0.002
20248	England	2010/11	B	B	9239	ST-103 complex	Blood	0.023	0.008	0.003	0.002
20249	England	2010/11	B	B	2632	ST-41/44 complex	CSF	0.047	0.012	0.003	0.002
20250	England	2010/11	B	B	2931	ST-32 complex	CSF	0.25	0.003	0.003	0.006
20251	England	2010/11	B	B	1194	ST-41/44 complex	Blood	0.19	0.006	0.003	0.004
20252	England	2010/11	B	B	213	ST-213 complex	Blood	0.064	0.012	0.003	0.003
20253	England	2010/11	B	B	8052	ST-41/44 complex	Blood	0.032	0.008	0.003	0.002
20255	Wales	2010/11	B	B	5981	ST-41/44 complex	Blood	0.125	0.032	0.003	0.006
20256	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.003	0.003
20257	England	2010/11	B	B	9821	ST-60 complex	Blood	0.094	0.008	0.003	0.002
20258	England	2010/11	B	B	437	ST-41/44 complex	Blood	0.064	0.004	0.003	0.003
20259	England	2010/11	B	B	213	ST-213 complex	Blood	0.064	0.012	0.003	0.003
20260	England	2010/11	B	B	4713	UA	Blood	0.064	0.003	0.003	0.003
20261	England	2010/11	B	B	3537	ST-11 complex	Blood	0.064	0.004	0.003	0.004
20263	England	2010/11	B	B	3818	ST-41/44 complex	Blood	0.047	0.006	0.003	<0.002
20264	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.064	0.003	0.003	0.003
20265	England	2010/11	B	B	4713	UA	Blood	0.094	0.008	0.003	0.003
20266	England	2010/11	B	B	282	ST-282 complex	Blood	0.047	0.012	0.003	0.003
20267	England	2010/11	B	B	162	ST-162 complex	Blood	0.5	0.032	0.004	0.25
20268	England	2010/11	B	B	269	ST-269 complex	Blood	0.064	0.008	0.004	0.004
20269	Wales	2010/11	B	B	18	ST-18 complex	Blood	0.047	0.008	0.003	0.004
20270	England	2010/11	B	B	213	ST-213 complex	CSF	0.19	0.006	0.003	0.004
20271	England	2010/11	B	B	213	ST-213 complex	Blood	0.064	0.012	0.003	0.003
20272	England	2010/11	B	B	1161	ST-269 complex	Blood	0.25	0.006	0.004	0.004
20273	England	2010/11	B	B	2080	ST-41/44 complex	Blood	0.023	0.003	0.002	0.002
20274	England	2010/11	B	B	275	ST-269 complex	CSF	0.064	0.008	0.003	0.003
20275	England	2010/11	B	B	213	ST-213 complex	Blood	0.094	0.008	0.003	0.004
20276	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.047	0.004	0.003	0.002
20277	England	2010/11	B	B	2314	ST-41/44 complex	Blood	0.25	0.003	0.003	0.004
20278	Wales	2010/11	B	B	7939	ST-269 complex	Blood	0.19	0.003	0.004	0.002
20279	England	2010/11	B	B	479	ST-269 complex	Blood	0.047	0.032	0.004	0.002
20280	England	2010/11	B	B	1475	ST-41/44 complex	CSF	0.19	0.003	0.003	0.003
20281	England	2010/11	Y	Y	10138	ST-23 complex	Blood	0.125	0.006	0.003	0.006
20282	England	2010/11	Y	Y	1466	ST-174 complex	Blood	0.125	0.023	0.003	0.004
20283	England	2010/11	B	B	327	ST-41/44 complex	Blood	0.19	0.004	0.003	0.004
20284	England	2010/11	B	B	5861	ST-41/44 complex	Blood	0.25	0.008	0.004	0.003
20285	England	2010/11	Y	Y	1466	ST-174 complex	Blood	0.125	0.008	0.003	0.006
20286	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.016	0.003	0.002	<0.002
20287	England	2010/11	B	B	9327	ST-60 complex	Blood	0.125	0.023	0.003	0.008
20289	England	2010/11	B	B	10139	ST-41/44 complex	Blood	0.032	0.047	0.003	0.002
20290	England	2010/11	B	B	5981	ST-41/44 complex	Blood	0.032	0.004	0.002	<0.002
20291	England	2010/11	B	B	35	ST-35 complex	Blood	0.064	0.004	0.003	0.003
20292	England	2010/11	B	B	33	ST-32 complex	Blood	0.064	0.008	0.003	0.003
20293	England	2010/11	B	B	3138	UA	Blood	0.19	0.008	0.002	0.004
20294	England	2010/11	B	B	1049	ST-269 complex	Blood	0.047	0.006	0.003	0.002
20295	England	2010/11	B	B	213	ST-213 complex	Blood	0.19	0.012	0.002	0.004
20296	Wales	2010/11	B	B	9834	UA	Blood	0.19	0.004	0.003	0.003
20297	England	2010/11	B	B	32	ST-32 complex	Blood	0.064	0.064	0.003	0.003
20299	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.19	0.004	0.003	0.004

20300	England	2010/11	B	B	8068	ST-282 complex	Blood	0.094	0.008	0.003	0.004
20301	England	2010/11	B	B	9892	ST-41/44 complex	Blood	0.094	0.008	0.003	0.002
20302	Wales	2010/11	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.002	0.004
20303	England	2010/11	B	B	1097	ST-41/44 complex	Blood	0.032	0.008	0.004	0.003
20304	England	2010/11	B	B	1475	ST-41/44 complex	Blood	0.023	0.006	0.003	<0.002
20305	Northern Ireland	2010/11	B	B	340	ST-41/44 complex	Blood	0.064	0.008	0.003	0.004
20306	England	2010/11	B	B	461	ST-461 complex	Blood	0.19	0.016	0.002	0.008
20307	England	2010/11	C	C	839	ST-41/44 complex	CSF	0.047	0.008	0.003	0.002
20308	England	2010/11	Y	Y	1466	ST-174 complex	Blood	0.125	0.008	0.002	0.003
20309	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.125	0.002	0.002	0.004
20310	Northern Ireland	2010/11	Y	Y	9893	ST-174 complex	Blood	0.094	0.006	<0.002	0.004
20312	England	2010/11	B	B	1194	ST-41/44 complex	Blood	0.032	0.004	0.003	0.002
20313	England	2010/11	B	B	1946	ST-461 complex	Blood	0.125	0.016	0.002	0.003
20314	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.002	0.003	0.003
20315	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.003	0.003
20317	England	2010/11	Y	Y	6463	ST-23 complex	Blood	0.064	0.003	0.002	0.004
20318	England	2010/11	W	W	184	ST-22 complex	Blood	0.19	0.047	0.004	0.003
20319	England	2010/11	B	B	35	ST-35 complex	Blood	0.047	0.004	0.003	0.002
20320	England	2010/11	NG	NG	9835	ST-226 complex	Blood	0.047	0.19	0.004	0.002
20321	England	2010/11	C	C	5238	UA	Blood	0.094	0.023	0.004	0.003
20322	England	2010/11	B	B	1161	ST-269 complex	CSF	0.094	0.008	0.004	0.004
20323	England	2010/11	B	B	3482	UA	Blood	0.047	0.006	0.002	0.003
20324	England	2010/11	B	B	1194	ST-41/44 complex	Blood	0.094	0.008	0.004	0.003
20325	England	2010/11	B	B	1194	ST-41/44 complex	Blood	0.064	0.004	0.004	0.003
20326	England	2010/11	B	B	9845	UA	Blood	0.064	0.006	0.004	0.004
20327	England	2010/11	B	B	1960	ST-41/44 complex	Blood	0.094	0.006	0.004	0.004
20328	England	2010/11	NG	E	60	ST-60 complex	PUS, HIP	0.032	0.004	0.003	0.003
20329	England	2010/11	C	C	11	ST-11 complex	CSF	0.064	0.125	0.004	0.003
20330	England	2010/11	B	B	1194	ST-41/44 complex	Blood	0.064	0.006	0.004	0.002
20331	England	2010/11	B	B	8944	UA	Blood	0.094	0.016	0.003	0.004
20333	England	2010/11	B	B	1090	ST-41/44 complex	Blood	0.19	0.008	0.003	0.002
20334	England	2010/11	B	B	9822	ST-41/44 complex	Blood	0.064	0.032	0.004	0.003
20335	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.064	0.002	0.003	0.004
20336	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.25	0.008	0.004	0.003
20337	England	2010/11	W	W	184	ST-22 complex	Blood	0.094	0.002	0.004	0.002
20338	England	2010/11	A	A	4789	ST-5 complex	Blood	0.047	0.125	0.5	0.003
20339	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.003	0.004
20340	England	2010/11	B	B	9836	ST-269 complex	Blood	0.047	0.008	0.004	0.002
20341	England	2010/11	B	B	213	ST-213 complex	Blood	0.064	0.016	0.004	0.003
20342	England	2010/11	B	B	213	ST-213 complex	Blood	0.19	0.008	0.003	0.004
20343	England	2010/11	B	B	1090	ST-41/44 complex	Blood	0.19	0.012	0.002	0.003
20344	England	2010/11	B	B	269	ST-269 complex	Blood	0.125	0.004	0.003	0.002
20345	England	2010/11	B	B	41	ST-41/44 complex	CSF	0.125	0.006	0.003	0.006
20346	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.003	0.004
20347	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.023	<0.002	0.002	0.003
20348	Northern Ireland	2010/11	B	B	278	ST-35 complex	Blood	0.25	0.008	0.002	0.006
20349	England	2010/11	B	B	275	ST-269 complex	CSF	0.064	0.003	0.002	0.003
20350	England	2010/11	B	B	213	ST-213 complex	Blood	0.19	0.016	0.003	0.006
20351	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.064	0.008	0.002	0.004
20352	England	2010/11	B	B	1161	ST-269 complex	CSF	0.19	0.006	0.003	0.006
20353	England	2010/11	B	B	33	ST-32 complex	Blood	0.032	0.003	0.003	0.004
20354	England	2010/11	B	B	9894	UA	Blood	0.064	0.016	0.002	0.006
20355	Northern Ireland	2010/11	B	B	9846	ST-865 complex	Blood	0.023	0.004	0.003	0.002
20356	Northern Ireland	2010/11	B	B	340	ST-41/44 complex	Blood	0.064	0.006	0.003	0.002
20357	England	2010/11	B	B	9895	ST-213 complex	Blood	0.064	0.004	0.002	0.003
20358	England	2010/11	B	B	2363	ST-41/44 complex	Blood	0.064	0.008	0.004	0.003
20359	England	2010/11	C	C	11	ST-11 complex	Joint	0.032	0.016	0.003	0.003
20360	England	2010/11	B	B	303	ST-41/44 complex	Blood	0.38	0.032	0.002	0.008
20361	England	2010/11	B	B	34	ST-32 complex	Blood	0.19	0.006	<0.002	0.008
20362	England	2010/11	B	B	213	ST-213 complex	Blood	0.047	0.006	0.002	0.003
20363	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.003
20364	England	2010/11	B	B	2314	ST-41/44 complex	Blood	0.125	0.002	0.002	0.003
20365	England	2010/11	W	W	184	ST-22 complex	Blood	0.19	0.003	0.004	0.004
20366	England	2010/11	B	B	275	ST-269 complex	Blood	0.25	0.004	0.003	0.006
20367	England	2010/11	B	B	2888	UA	Blood	0.064	0.008	0.004	0.003
20369	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.25	0.008	0.003	0.006
20370	England	2010/11	B	B	9837	UA	Blood	0.19	0.003	0.003	0.006
20371	England	2010/11	B	B	9896	ST-41/44 complex	Blood	0.064	0.004	0.002	0.002
20372	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.064	0.004	0.003	0.004
20373	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.002	0.004
20374	England	2010/11	B	B	1161	ST-269 complex	Blood	0.19	0.006	0.002	0.004
20375	England	2010/11	B	B	1161	ST-269 complex	Blood	0.25	0.012	0.003	0.004
20376	England	2010/11	B	B	479	ST-269 complex	Blood	0.047	0.006	0.003	0.003
20377	England	2010/11	B	B	269	ST-269 complex	Blood	0.047	0.004	0.003	0.002
20378	Northern Ireland	2010/11	B	B	9004	ST-269 complex	Blood	0.047	0.006	0.003	0.003
20379	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.002	0.004
20380	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.003	0.008
20381	England	2010/11	B	B	9847	UA	Blood	0.064	0.008	0.004	0.006
20382	England	2010/11	C	C	32	ST-32 complex	Blood	0.064	0.006	0.003	0.003
20383	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.003	0.003
20384	England	2010/11	B	B	1194	ST-41/44 complex	Blood	0.19	0.016	0.003	0.004
20385	England	2010/11	B	B	1161	ST-269 complex	Blood	0.094	0.006	0.003	0.004
20386	England	2010/11	B	B	833	ST-41/44 complex	Blood	0.047	0.004	0.003	0.002
20387	England	2010/11	B	B	6604	ST-269 complex	Blood	0.25	0.004	0.003	0.008
20388	England	2010/11	B	B	162	ST-162 complex	Blood	0.047	0.003	0.003	0.003

20389	England	2010/11	B	B	213	ST-213 complex	Blood	0.047	0.004	0.002	0.003
20390	England	2010/11	B	B	3737	ST-1157 complex	Blood	0.125	0.004	0.002	0.006
20391	England	2010/11	B	B	60	ST-60 complex	Blood	0.19	0.004	0.002	0.004
20393	England	2010/11	B	B	32	ST-32 complex	Blood	0.064	0.006	0.003	0.003
20394	England	2010/11	B	B	1200	ST-41/44 complex	Blood	0.047	0.006	0.004	0.002
20395	England	2010/11	B	B	213	ST-213 complex	CSF	0.19	0.012	0.003	0.008
20396	England	2010/11	Y	Y	168	ST-167 complex	Blood	0.064	0.004	0.003	0.004
20397	England	2010/11	C	C	5133	ST-103 complex	Blood	0.016	0.006	0.002	<0.002
20400	England	2010/11	B	B	9838	ST-41/44 complex	CSF	0.19	0.006	0.004	0.006
20401	England	2010/11	B	B	1161	ST-269 complex	Blood	0.064	0.008	0.003	0.008
20402	England	2010/11	B	B	275	ST-269 complex	Blood	0.064	0.003	0.004	0.004
20403	England	2010/11	B	B	32	ST-32 complex	Blood	0.047	0.012	0.003	0.003
20404	England	2010/11	W/Y	W/Y	23	ST-23 complex	Blood	0.38	0.008	0.003	0.023
20405	England	2010/11	B	B	180	ST-41/44 complex	CSF	0.023	0.004	0.002	0.002
20406	England	2010/11	C	C	5315	UA	CSF	0.016	0.012	0.003	0.006
20407	England	2010/11	B	B	154	ST-41/44 complex	Blood	0.047	0.012	0.003	0.006
20408	England	2010/11	B	B	41	ST-41/44 complex	CSF	0.047	0.006	0.003	0.002
20409	Northern Ireland	2010/11	B	B	33	ST-32 complex	Blood	0.064	0.003	0.003	0.003
20410	England	2010/11	B	B	46	ST-41/44 complex	Blood	0.047	0.012	0.002	<0.002
20411	England	2010/11	B	B	269	ST-269 complex	Blood	0.047	0.012	0.004	0.003
20412	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.25	0.004	0.003	0.008
20413	England	2010/11	B	B	162	ST-162 complex	Blood	0.064	0.094	0.004	0.004
20414	England	2010/11	NG	Y	1655	ST-23 complex	Blood	0.032	0.003	0.003	0.002
20415	England	2010/11	B	B	1194	ST-41/44 complex	CSF	0.064	0.004	0.003	0.003
20416	England	2010/11	B	B	269	ST-269 complex	Blood	0.032	0.008	0.003	0.002
20417	England	2010/11	B	B	269	ST-269 complex	Blood	0.19	0.002	0.003	0.004
20418	England	2010/11	B	B	162	ST-162 complex	Blood	0.094	0.016	0.004	0.004
20419	England	2010/11	B	B	485	ST-41/44 complex	Joint	0.25	0.003	0.003	0.004
20420	England	2010/11	B	B	3077	ST-35 complex	Blood	0.047	0.023	0.003	0.002
20421	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.19	0.006	0.003	0.004
20422	England	2010/11	W	W	184	ST-22 complex	Blood	0.125	0.004	0.003	0.003
20423	England	2010/11	B	B	9823	ST-269 complex	Blood	0.047	0.006	0.003	0.002
20425	England	2010/11	B	B	1159	UA	CSF	0.047	0.003	0.003	0.003
20426	England	2010/11	B	B	9824	ST-41/44 complex	Blood	0.047	0.004	0.003	0.002
20427	England	2010/11	B	B	290	ST-32 complex	Blood	0.064	0.006	0.003	0.004
20428	England	2010/11	B	B	5103	ST-60 complex	Blood	0.064	0.006	0.003	0.003
20429	England	2010/11	B	B	1163	ST-269 complex	Blood	0.064	0.006	0.002	0.004
20430	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.002	0.002	0.004
20431	England	2010/11	B	B	1161	ST-269 complex	Blood	0.047	0.006	0.003	0.003
20432	Wales	2010/11	B	B	41	ST-41/44 complex	Blood	0.064	0.032	0.003	0.003
20433	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.003	0.003
20434	England	2010/11	B	B	1161	ST-269 complex	CSF	0.125	0.008	0.003	0.006
20435	England	2010/11	B	B	9825	UA	Blood	0.25	0.008	0.002	0.012
20437	England	2010/11	B	B	1161	ST-269 complex	Blood	0.094	0.012	0.003	0.004
20438	England	2010/11	B	B	32	ST-32 complex	Blood	0.047	0.004	0.003	0.003
20439	England	2010/11	B	B	269	ST-269 complex	Blood	0.047	0.016	0.004	0.002
20440	England	2010/11	Y	Y	4183	ST-23 complex	Blood	0.094	0.023	0.002	0.008
20441	England	2010/11	B	B	1430	ST-60 complex	Blood	0.032	0.004	0.002	0.002
20442	England	2010/11	B	B	9826	ST-269 complex	Blood	0.064	0.008	0.003	0.004
20443	England	2010/11	B	B	5551	ST-41/44 complex	Blood	0.016	0.016	<0.002	<0.002
20445	England	2010/11	B	B	41	ST-41/44 complex	CSF	0.19	0.004	0.003	0.008
20446	England	2010/11	B	B	467	ST-269 complex	Blood	0.047	0.004	0.003	0.002
20447	England	2010/11	B	B	3101	ST-41/44 complex	Blood	0.047	0.006	0.003	0.003
20448	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.19	0.006	0.003	0.004
20450	England	2010/11	B	B	275	ST-269 complex	CSF	0.047	0.004	0.003	0.003
20451	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.064	0.006	0.002	0.003
20452	England	2010/11	B	B	9827	UA	Blood	0.047	0.004	0.003	0.003
20453	England	2010/11	B	B	1194	ST-41/44 complex	CSF	0.047	0.006	0.003	0.002
20454	England	2010/11	Y	Y	1655	ST-23 complex	Blood	0.125	0.004	0.003	0.008
20455	England	2010/11	B	B	1161	ST-269 complex	Blood	0.094	0.016	0.003	0.003
20456	Northern Ireland	2010/11	Y	Y	784	ST-92 complex	Blood	0.094	0.004	0.003	0.003
20457	England	2010/11	B	B	60	ST-60 complex	Blood	0.032	0.002	0.003	<0.002
20458	England	2010/11	W	W	2977	ST-174 complex	Blood	0.125	0.008	0.002	0.008
20459	England	2010/11	Y	Y	23	ST-23 complex	Blood	0.064	0.003	0.006	0.004
20470	England	2010/11	B	B	41	ST-41/44 complex	Blood	0.19	0.008	0.003	0.004
21092	England	2011/12	B	B	461	ST-461 complex	Blood	0.125	0.008	0.002	0.003
21093	England	2011/12	B	B	1161	ST-269 complex	Blood	0.064	0.047	0.004	0.003
21094	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.003	0.004
21095	England	2011/12	B	B	1960	ST-41/44 complex	Blood	0.064	0.012	0.004	0.003
21096	Wales	2011/12	B	B	8049	ST-32 complex	Blood	0.25	0.004	0.003	0.003
21097	England	2011/12	B	B	1161	ST-269 complex	CSF	0.094	0.012	0.003	0.004
21098	England	2011/12	B	B	1194	ST-41/44 complex	Blood	0.047	0.006	0.002	0.003
21099	England	2011/12	B	B	213	ST-213 complex	Blood	0.125	0.016	0.003	0.004
21100	England	2011/12	B	B	275	ST-269 complex	CSF	0.25	0.023	0.003	0.006
21101	England	2011/12	B	B	2391	ST-213 complex	Blood	0.047	0.006	0.003	0.004
21102	England	2011/12	B	B	9200	ST-41/44 complex	Blood	0.047	0.006	0.003	0.006
21103	England	2011/12	B	B	1163	ST-269 complex	Blood	0.125	0.006	0.003	0.004
21104	Wales	2011/12	B	B	6428	ST-269 complex	Blood	0.094	0.012	0.004	0.006
21105	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.094	0.004	0.003	0.008
21106	England	2011/12	B	B	1161	ST-269 complex	CSF	0.064	0.004	0.004	0.004
21107	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.003	0.004
21108	England	2011/12	Y	Y	8096	ST-23 complex	Blood	0.19	0.004	0.004	0.003
21109	England	2011/12	B	B	162	ST-162 complex	Blood	0.064	0.032	0.004	0.004
21110	England	2011/12	B	B	10260	ST-11 complex	Blood	0.19	0.012	0.004	0.008
21111	England	2011/12	B	B	213	ST-213 complex	Blood	0.023	0.008	0.002	0.002

21112	England	2011/12	B	B	60	ST-60 complex	Blood	0.047	0.032	0.004	0.004
21113	England	2011/12	B	B	2009	ST-41/44 complex	Blood	0.064	0.004	0.004	0.003
21114	England	2011/12	B	B	485	ST-41/44 complex	Blood	0.19	0.004	0.004	0.004
21115	Northern Ireland	2011/12	C	C	10261	UA	Blood	0.032	0.004	0.003	0.003
21116	England	2011/12	B	B	4051	UA	Blood	0.032	0.032	0.003	0.002
21117	England	2011/12	B	B	1097	ST-41/44 complex	Blood	0.047	0.004	0.006	0.003
21118	England	2011/12	B	B	467	ST-269 complex	Blood	0.064	0.006	0.003	0.004
21119	England	2011/12	B	B	162	ST-162 complex	Blood	0.023	0.016	0.004	0.004
21120	England	2011/12	B	B	269	ST-269 complex	Blood	0.032	0.008	0.004	0.004
21121	England	2011/12	B	B	1163	ST-269 complex	Blood	0.19	0.004	0.004	0.008
21122	England	2011/12	B	B	2799	ST-41/44 complex	CSF	0.125	0.008	0.004	0.008
21124	England	2011/12	B	B	10262	UA	CSF	0.25	0.006	0.003	0.016
21125	England	2011/12	B	B	4237	ST-865 complex	Blood	0.047	0.016	0.004	0.004
21126	England	2011/12	B	B	213	ST-213 complex	Blood	0.032	0.008	0.003	0.003
21127	England	2011/12	B	B	3050	ST-41/44 complex	BRAIN	0.094	0.003	0.002	0.003
21128	England	2011/12	B	B	9822	ST-41/44 complex	Blood	0.064	0.008	0.003	0.004
21129	England	2011/12	B	B	154	ST-41/44 complex	Blood	0.016	0.002	0.003	<0.002
21130	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.003	0.004
21131	England	2011/12	B	B	259	ST-32 complex	Blood	0.094	0.012	0.003	0.006
21132	England	2011/12	W	W	1281	ST-22 complex	Blood	0.25	0.016	0.006	0.008
21133	England	2011/12	B	B	10263	UA	Blood	0.125	0.016	0.006	0.012
21134	England	2011/12	C	C	11	ST-11 complex	Blood	0.047	0.032	0.004	0.004
21137	England	2011/12	B	B	8988	UA	Blood	0.19	0.012	0.004	0.006
21138	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.004
21139	England	2011/12	W	W	184	ST-22 complex	Joint	0.125	0.004	0.004	0.004
21140	England	2011/12	B	B	1163	ST-269 complex	Blood	0.032	0.008	0.003	0.003
21141	England	2011/12	B	B	213	ST-213 complex	CSF	0.19	0.125	0.002	0.008
21142	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.125	0.008	0.003	0.004
21143	England	2011/12	B	B	10264	ST-269 complex	Blood	0.047	0.023	<0.002	0.003
21144	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.25	0.023	0.004	0.006
21145	England	2011/12	B	B	213	ST-213 complex	Blood	0.064	0.023	0.003	0.004
21146	England	2011/12	B	B	1161	ST-269 complex	Blood	0.047	0.016	0.003	0.004
21147	England	2011/12	B	B	213	ST-213 complex	Joint	0.047	0.008	0.003	0.004
21148	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.003	0.004
21151	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.016	0.002	0.003	0.003
21152	England	2011/12	B	B	1097	ST-41/44 complex	CSF	0.047	0.006	0.003	0.004
21153	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.004
21154	Wales	2011/12	B	B	5906	ST-41/44 complex	Blood	0.19	0.006	0.003	0.004
21155	England	2011/12	B	B	6781	UA	Blood	0.25	0.032	0.003	0.012
21156	England	2011/12	W	W	3795	ST-22 complex	Blood	0.125	0.004	0.004	0.004
21157	Northern Ireland	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.004	0.004
21158	England	2011/12	Y	Y	3582	ST-23 complex	Blood	0.094	0.004	0.003	0.008
21159	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.19	0.008	0.003	0.004
21160	England	2011/12	B	B	1345	UA	Blood	0.064	0.016	0.003	0.004
21161	England	2011/12	B	B	5357	ST-41/44 complex	Blood	0.032	0.006	0.003	0.003
21162	England	2011/12	B	B	275	ST-269 complex	Blood	0.064	0.003	0.003	0.004
21164	England	2011/12	B	B	213	ST-213 complex	Blood	0.25	0.008	0.003	0.006
21165	England	2011/12	B	B	9889	ST-41/44 complex	Blood	0.125	0.008	0.003	0.006
21167	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	<0.002	0.006
21168	England	2011/12	B	B	1161	ST-269 complex	Blood	0.125	0.006	0.003	0.006
21169	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.094	0.004	0.003	0.008
21170	England	2011/12	B	B	6604	ST-269 complex	Blood	0.064	0.006	0.004	0.004
21171	England	2011/12	B	B	1097	ST-41/44 complex	Blood	0.047	0.016	0.004	0.003
21172	Wales	2011/12	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.003	0.003
21173	England	2011/12	B	B	213	ST-213 complex	Blood	0.064	0.008	0.003	0.004
21174	England	2011/12	B	B	10265	UA	Blood	0.047	0.008	0.003	0.002
21175	England	2011/12	W	W	1286	ST-22 complex	Blood	0.19	0.016	0.003	0.006
21176	England	2011/12	B	B	35	ST-35 complex	Blood	0.047	0.064	0.002	0.003
21177	England	2011/12	B	B	162	ST-162 complex	Blood	0.25	0.008	0.003	0.006
21178	England	2011/12	Y	Y	8411	ST-23 complex	PUS, HIP	0.064	0.004	0.003	0.003
21179	England	2011/12	B	B	749	ST-32 complex	Blood	0.19	0.003	0.004	0.008
21180	England	2011/12	B	B	1942	ST-269 complex	Blood	0.047	0.016	0.004	0.003
21181	England	2011/12	B	B	275	ST-269 complex	Blood	0.19	0.006	0.003	0.004
21182	England	2011/12	B	B	10266	UA	Blood	0.125	0.006	0.003	0.008
21183	England	2011/12	Y	Y	1655	ST-23 complex	Joint	0.047	0.003	0.003	0.004
21184	England	2011/12	B	B	8054	ST-41/44 complex	Blood	0.064	0.008	0.004	0.003
21186	England	2011/12	B	B	18	ST-18 complex	Blood	0.032	0.047	0.003	0.003
21187	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.016	0.003	<0.002	<0.002
21188	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.047	0.023	0.003	0.003
21189	England	2011/12	B	B	269	ST-269 complex	Blood	0.064	0.012	0.003	0.003
21190	England	2011/12	B	B	283	ST-269 complex	Blood	0.047	0.008	0.003	0.002
21191	England	2011/12	B	B	1161	ST-269 complex	CSF	0.064	0.008	0.003	0.004
21192	England	2011/12	Y	Y	6463	ST-23 complex	Blood	0.047	0.008	0.003	0.004
21193	England	2011/12	W/Y	W/Y	3651	ST-22 complex	Blood	0.047	0.012	0.004	0.003
21194	England	2011/12	B	B	269	ST-269 complex	Blood	0.064	0.012	0.003	0.003
21195	Northern Ireland	2011/12	B	B	4496	ST-41/44 complex	Blood	0.032	0.008	0.003	0.003
21196	England	2011/12	C	C	11	ST-11 complex	Blood	0.047	0.004	0.003	0.003
21198	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.003
21199	England	2011/12	B	B	103	ST-103 complex	CSF	0.094	0.008	0.003	0.003
21200	England	2011/12	B	B	136	ST-41/44 complex	CSF	0.094	0.004	0.002	0.004
21201	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.032	0.006	0.003	0.002
21202	England	2011/12	B	B	269	ST-269 complex	Blood	0.032	0.012	0.003	0.003
21203	Wales	2011/12	W	W	11	ST-11 complex	Blood	0.064	0.016	0.004	0.004
21204	England	2011/12	B	B	33	ST-32 complex	Blood	0.047	0.008	0.004	0.004
21205	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.047	0.003	0.003	0.003

21207	Northern Ireland	2011/12	B	B	1163	ST-269 complex	Blood	0.19	0.012	0.002	0.003
21208	England	2011/12	C	C	11	ST-11 complex	Blood	0.19	0.047	0.003	0.004
21209	England	2011/12	B	B	275	ST-269 complex	CSF	0.047	0.004	0.003	0.003
21210	England	2011/12	B	B	340	ST-41/44 complex	Blood	0.032	0.006	0.003	<0.002
21211	England	2011/12	B	B	1161	ST-269 complex	Blood	0.094	0.006	0.003	0.006
21212	England	2011/12	B	B	213	ST-213 complex	CSF	0.047	0.006	0.003	0.003
21213	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.19	0.006	0.003	0.004
21214	Wales	2011/12	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.004
21215	England	2011/12	B	B	1161	ST-269 complex	Blood	0.064	0.008	0.003	0.003
21217	England	2011/12	B	B	213	ST-213 complex	Blood	0.047	0.012	0.003	0.003
21218	England	2011/12	B	B	213	ST-213 complex	Blood	0.032	0.004	0.003	0.003
21219	England	2011/12	B	B	13	ST-269 complex	Blood	0.047	0.008	0.004	0.003
21220	England	2011/12	B	B	275	ST-269 complex	Blood	0.064	0.008	0.003	0.003
21221	Wales	2011/12	B	B	10267	ST-213 complex	CSF	0.047	0.016	0.002	0.003
21222	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.032	0.004	0.003	0.002
21223	Northern Ireland	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.002	0.002
21224	England	2011/12	B	B	1159	UA	Blood	0.032	0.012	0.003	0.003
21225	England	2011/12	B	B	32	ST-32 complex	Blood	0.047	0.016	0.003	0.003
21226	England	2011/12	B	B	1161	ST-269 complex	Blood	0.094	0.004	0.003	0.004
21227	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.094	0.006	0.002	0.006
21228	England	2011/12	B	B	461	ST-461 complex	Blood	0.125	0.006	0.002	0.004
21229	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.002	0.004
21230	England	2011/12	B	B	1194	ST-41/44 complex	CSF	0.047	0.006	0.003	0.003
21231	England	2011/12	B	B	7226	ST-269 complex	Blood	0.032	0.004	0.002	0.003
21232	England	2011/12	C	C	11	ST-11 complex	Blood	0.032	0.016	0.003	0.003
21233	England	2011/12	B	B	1161	ST-269 complex	Blood	0.064	0.032	0.003	0.004
21234	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.047	0.032	0.002	0.003
21235	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.064	0.004	0.003	0.003
21236	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.125	0.004	0.003	0.004
21237	England	2011/12	B	B	11	ST-11 complex	Blood	0.064	0.016	0.003	0.004
21238	Wales	2011/12	B	B	1194	ST-41/44 complex	Blood	0.047	0.004	0.003	0.003
21239	England	2011/12	B	B	33	ST-32 complex	Blood	0.125	0.003	0.002	0.004
21240	England	2011/12	B	B	5529	ST-18 complex	CSF	0.032	0.016	0.003	0.003
21241	England	2011/12	B	B	269	ST-269 complex	Joint	0.064	0.012	0.003	0.004
21242	England	2011/12	B	B	6605	ST-35 complex	Blood	0.016	<0.002	<0.002	<0.002
21243	England	2011/12	B	B	10268	ST-1157 complex	Blood	0.047	0.006	0.002	0.004
21244	England	2011/12	B	B	1161	ST-269 complex	Blood	0.047	0.006	0.003	0.003
21245	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.125	0.003	0.003	0.004
21246	England	2011/12	B	B	461	ST-461 complex	Blood	0.19	0.006	0.002	0.006
21247	England	2011/12	B	B	485	ST-41/44 complex	Blood	0.19	0.006	0.003	0.004
21248	England	2011/12	B	B	269	ST-269 complex	Blood	0.047	0.006	0.003	0.003
21249	England	2011/12	B	B	282	ST-282 complex	Blood	0.047	0.012	0.002	0.003
21250	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.002	0.004
21252	England	2011/12	B	B	1157	ST-1157 complex	Blood	0.047	0.012	<0.002	0.004
21253	England	2011/12	C	C	11	ST-11 complex	Blood	0.25	0.012	0.003	0.008
21254	England	2011/12	B	B	10269	ST-41/44 complex	Blood	0.25	0.006	0.004	0.006
21255	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.002	0.004
21256	England	2011/12	C	C	11	ST-11 complex	Blood	0.25	0.023	0.003	0.008
21257	England	2011/12	B	B	1194	ST-41/44 complex	Blood	0.032	0.008	0.003	0.003
21258	Northern Ireland	2011/12	B	B	10270	ST-41/44 complex	CSF	0.047	0.008	0.003	0.003
21259	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.003	0.003
21260	England	2011/12	B	B	275	ST-269 complex	Blood	0.064	0.008	0.003	0.004
21261	England	2011/12	B	B	1194	ST-41/44 complex	Blood	0.047	0.008	0.002	0.002
21262	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.064	0.004	0.003	0.004
21263	England	2011/12	B	B	1194	ST-41/44 complex	Blood	0.047	0.006	0.003	0.002
21264	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.047	0.023	0.003	0.003
21265	England	2011/12	B	B	32	ST-32 complex	Blood	0.19	0.094	0.003	0.004
21266	England	2011/12	B	B	162	ST-162 complex	Blood	0.064	0.012	0.004	0.004
21267	England	2011/12	B	B	10271	ST-1157 complex	Blood	0.016	0.016	0.002	0.002
21268	Northern Ireland	2011/12	B	B	575	ST-213 complex	CSF	0.19	0.006	0.003	0.004
21269	England	2011/12	B	B	1049	ST-269 complex	Blood	0.032	0.003	0.003	0.003
21270	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.125	0.006	0.002	0.004
21271	England	2011/12	Y	Y	3651	ST-22 complex	Blood	0.047	0.004	0.004	0.004
21272	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.125	0.006	0.003	0.008
21273	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.25	0.016	0.003	0.006
21274	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.004
21275	England	2011/12	B	B	213	ST-213 complex	Blood	0.047	0.012	0.002	0.003
21276	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.012	0.003	<0.002	0.002
21277	England	2011/12	B	B	8988	UA	Blood	0.125	0.012	0.003	0.003
21278	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.125	0.006	0.003	0.004
21279	England	2011/12	B	B	1163	ST-269 complex	Blood	0.125	0.012	<0.002	0.003
21280	Wales	2011/12	B	B	60	ST-60 complex	Blood	0.032	0.006	0.002	0.003
21281	England	2011/12	B	B	10272	ST-213 complex	Blood	0.047	0.016	0.003	0.002
21282	England	2011/12	B	B	1161	ST-269 complex	Blood	0.094	0.012	0.003	0.004
21283	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.004
21284	England	2011/12	B	B	213	ST-213 complex	CSF	0.064	0.016	0.003	0.004
21285	England	2011/12	B	B	1161	ST-269 complex	CSF	0.064	0.008	0.003	0.003
21286	England	2011/12	B	B	7385	ST-41/44 complex	Blood	0.19	0.004	0.004	0.004
21287	England	2011/12	B	B	1161	ST-269 complex	Blood	0.094	0.004	0.003	0.004
21288	Wales	2011/12	W	W	11	ST-11 complex	Blood	0.047	0.012	0.006	0.003
21289	England	2011/12	B	B	1161	ST-269 complex	Blood	0.064	0.008	0.004	0.004
21290	England	2011/12	W	W	184	ST-22 complex	Blood	0.19	0.016	0.006	0.004
21291	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.004	0.003
21292	England	2011/12	B	B	154	ST-41/44 complex	Blood	0.032	0.003	0.003	0.002
21293	England	2011/12	Y	Y	23	ST-23 complex	Joint	0.064	0.004	0.003	0.003

21294	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.003
21295	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.003	0.003
21296	England	2011/12	C	C	877	ST-41/44 complex	Blood	0.125	0.004	0.004	0.004
21299	England	2011/12	B	B	154	ST-41/44 complex	Blood	0.094	0.012	0.003	0.004
21300	England	2011/12	B	B	461	ST-461 complex	CSF	0.023	0.023	0.003	<0.002
21301	Wales	2011/12	B	B	3754	ST-41/44 complex	Blood	0.047	0.003	0.004	0.003
21303	England	2011/12	B	B	213	ST-213 complex	CSF	0.047	0.012	0.004	0.003
21304	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.006
21306	England	2011/12	B	B	213	ST-213 complex	Blood	0.064	0.008	0.004	0.004
21307	Wales	2011/12	B	B	1161	ST-269 complex	Blood	0.094	0.008	0.004	0.006
21308	England	2011/12	B	B	275	ST-269 complex	Blood	0.19	0.012	0.004	0.006
21309	England	2011/12	B	B	162	ST-162 complex	Blood	0.064	0.012	0.004	0.004
21311	Wales	2011/12	B	B	11	ST-11 complex	Blood	0.064	0.012	0.003	0.004
21312	England	2011/12	B	B	1774	ST-269 complex	Blood	0.047	0.006	0.003	0.004
21313	England	2011/12	B	B	1194	ST-41/44 complex	Blood	0.047	0.004	0.003	0.003
21314	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.047	0.003	0.004	0.003
21315	England	2011/12	B	B	162	ST-162 complex	Blood	0.064	0.008	0.004	0.004
21316	England	2011/12	B	B	154	ST-41/44 complex	Blood	0.047	0.006	0.004	0.003
21317	England	2011/12	B	B	1049	ST-269 complex	Blood	0.032	0.006	0.004	0.002
21318	Wales	2011/12	B	B	3754	ST-41/44 complex	Blood	0.047	0.003	0.002	0.003
21319	Wales	2011/12	B	B	41	ST-41/44 complex	Blood	0.064	0.19	0.004	0.003
21320	England	2011/12	B	B	10273	UA	CSF	0.064	0.008	0.004	0.004
21321	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.064	0.004	0.004	0.004
21322	England	2011/12	B	B	1161	ST-269 complex	CSF	0.125	0.006	0.006	0.006
21323	England	2011/12	B	B	10274	ST-213 complex	Blood	0.19	0.032	0.003	0.004
21324	England	2011/12	B	B	10275	UA	Blood	0.047	0.125	0.003	0.004
21325	England	2011/12	B	B	162	ST-162 complex	Blood	0.047	0.016	0.004	0.003
21326	England	2011/12	B	B	32	ST-32 complex	Blood	0.047	0.012	0.004	0.003
21327	England	2011/12	B	B	269	ST-269 complex	Blood	0.064	0.012	0.004	0.002
21328	England	2011/12	B	B	32	ST-32 complex	Blood	0.047	0.004	0.004	0.003
21329	England	2011/12	B	B	1161	ST-269 complex	CSF	0.094	0.047	0.004	0.004
21330	Wales	2011/12	B	B	11	ST-11 complex	Blood	0.064	0.032	0.006	0.006
21331	England	2011/12	B	B	10276	ST-18 complex	Joint	0.032	0.032	0.004	0.003
21332	England	2011/12	B	B	3635	ST-213 complex	CSF	0.047	0.016	0.003	0.004
21333	England	2011/12	B	B	269	ST-269 complex	Blood	0.064	0.047	0.006	0.004
21335	England	2011/12	B	B	11	ST-11 complex	Blood	0.064	0.016	0.004	0.004
21336	England	2011/12	B	B	10277	UA	Blood	0.064	0.023	0.006	0.004
21337	England	2011/12	B	B	10278	ST-41/44 complex	Joint	0.094	0.006	0.004	0.003
21338	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.003
21339	England	2011/12	Y	Y	1466	ST-174 complex	Blood	0.125	0.047	0.003	0.006
21341	England	2011/12	B	B	1194	ST-41/44 complex	Blood	0.19	0.004	0.003	0.003
21342	England	2011/12	B	B	1161	ST-269 complex	Blood	0.125	0.006	0.004	0.006
21343	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.003	0.003
21344	England	2011/12	B	B	9352	ST-41/44 complex	Tissue	0.19	0.004	0.004	0.003
21345	England	2011/12	B	B	10279	ST-213 complex	Blood	0.19	0.125	0.004	0.003
21346	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.002
21347	England	2011/12	B	B	10280	ST-41/44 complex	Blood	0.032	0.012	0.003	0.002
21348	England	2011/12	B	B	1049	ST-269 complex	Blood	0.047	0.006	0.004	0.003
21349	England	2011/12	W	W	1224	ST-22 complex	Blood	0.125	0.004	0.004	0.002
21350	England	2011/12	B	B	1163	ST-269 complex	Blood	0.19	0.004	0.004	0.004
21351	England	2011/12	B	B	3496	ST-213 complex	Blood	0.125	0.064	0.004	0.004
21352	England	2011/12	E	E	4146	ST-60 complex	Blood	0.032	0.008	0.004	0.002
21353	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.125	0.006	0.003	0.004
21355	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.023	0.008	0.004	0.004
21356	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.023	0.004	0.004	0.002
21357	England	2011/12	B	B	1163	ST-269 complex	Blood	0.047	0.003	0.004	0.004
21358	England	2011/12	B	B	269	ST-269 complex	Blood	0.032	0.004	0.004	0.003
21359	England	2011/12	C	C	11	ST-11 complex	Blood	0.016	0.047	0.006	0.002
21360	England	2011/12	B	B	6058	ST-41/44 complex	CSF	0.19	0.012	0.004	0.006
21362	England	2011/12	B	B	1161	ST-269 complex	Blood	0.25	0.016	0.004	0.008
21363	England	2011/12	B	B	10281	ST-213 complex	Blood	0.047	0.008	0.003	0.004
21364	England	2011/12	C	C	11	ST-11 complex	Blood	0.023	0.016	0.006	0.003
21365	England	2011/12	B	B	7309	ST-213 complex	Blood	0.064	0.008	0.004	0.004
21366	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.003	0.003
21367	England	2011/12	B	B	1195	ST-269 complex	Blood	0.023	0.008	0.004	0.003
21368	Wales	2011/12	B	B	340	ST-41/44 complex	Blood	0.19	0.008	0.006	0.012
21369	Wales	2011/12	B	B	10282	ST-41/44 complex	Blood	0.19	0.012	0.004	0.004
21370	Northern Ireland	2011/12	B	B	10283	UA	Blood	0.19	0.004	0.004	0.004
21371	England	2011/12	W	W	184	ST-22 complex	Blood	0.125	0.016	0.006	0.004
21372	England	2011/12	Y	Y	1655	ST-23 complex	CSF	0.016	0.003	0.003	0.003
21373	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.032	0.003	0.003	0.006
21374	Wales	2011/12	B	B	41	ST-41/44 complex	Blood	0.032	0.008	0.003	0.002
21376	England	2011/12	B	B	1194	ST-41/44 complex	Blood	0.032	0.003	0.004	0.003
21378	England	2011/12	B	B	46	ST-41/44 complex	Blood	0.032	0.006	0.006	0.003
21380	England	2011/12	W	W	184	ST-22 complex	Blood	0.19	0.008	0.006	0.006
21382	England	2011/12	B	B	9171	ST-41/44 complex	Blood	0.047	0.006	0.004	0.004
21383	Wales	2011/12	B	B	1157	ST-1157 complex	CSF	0.016	0.003	0.003	0.003
21384	England	2011/12	B	B	1097	ST-41/44 complex	Blood	0.032	0.003	0.004	0.004
21385	England	2011/12	B	B	213	ST-213 complex	Blood	0.032	0.006	0.004	0.003
21387	England	2011/12	B	B	213	ST-213 complex	Blood	0.047	0.023	0.004	0.008
21388	England	2011/12	B	B	10285	ST-32 complex	Blood	0.064	0.008	0.004	0.006
21390	England	2011/12	B	B	10286	ST-32 complex	Blood	0.25	0.008	0.004	0.006
21391	England	2011/12	B	B	2307	UA	Blood	0.19	0.004	0.003	0.004
21392	England	2011/12	B	B	213	ST-213 complex	Blood	0.023	0.012	0.003	<0.002
21393	England	2011/12	B	B	269	ST-269 complex	Blood	0.047	0.003	0.004	0.003

21394	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.032	0.003	0.003	0.002
21396	England	2011/12	B	B	10287	ST-60 complex	Blood	0.064	0.004	0.004	0.004
21398	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.064	0.003	0.003	0.002
21399	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.032	<0.002	0.006	0.003
21400	England	2011/12	B	B	1194	ST-41/44 complex	Blood	0.125	0.003	0.003	0.003
21401	England	2011/12	B	B	43	ST-41/44 complex	CSF	0.047	0.003	0.004	0.003
21402	England	2011/12	NG	B	414	ST-41/44 complex	Blood	0.064	0.002	0.004	0.003
21403	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.023	<0.002	0.004	0.003
21404	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.094	0.002	0.006	0.008
21405	England	2011/12	B	B	1163	ST-269 complex	CSF	0.125	0.004	0.006	0.006
21406	Wales	2011/12	B	B	10288	ST-269 complex	CSF	0.064	0.006	0.006	0.004
21407	England	2011/12	C	C	11	ST-11 complex	Blood	0.023	0.012	0.006	0.003
21408	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.032	0.003	0.004	0.003
21410	Wales	2011/12	Y	Y	23	ST-23 complex	Blood	0.047	0.004	0.006	0.002
21411	England	2011/12	B	B	6782	ST-41/44 complex	Blood	0.032	0.012	0.006	0.003
21412	England	2011/12	B	B	2314	ST-41/44 complex	Blood	0.094	0.002	0.006	0.003
21413	England	2011/12	B	B	10289	ST-18 complex	Blood	0.064	0.016	0.004	0.006
21414	England	2011/12	B	B	6058	ST-41/44 complex	CSF	0.19	0.008	0.006	0.006
21415	England	2011/12	B	B	5151	UA	Blood	0.125	0.004	0.006	0.004
21416	England	2011/12	B	B	162	ST-162 complex	CSF	0.032	0.094	0.006	0.002
21417	England	2011/12	C	C	5133	ST-103 complex	Blood	0.012	0.003	0.006	<0.002
21418	England	2011/12	B	B	269	ST-269 complex	Blood	0.023	0.003	0.006	<0.002
21419	England	2011/12	C	C	11	ST-11 complex	Blood	0.125	0.016	0.006	0.006
21420	England	2011/12	B	B	162	ST-162 complex	Blood	0.125	0.008	0.006	0.006
21421	England	2011/12	Y	Y	1466	ST-174 complex	Blood	0.064	0.016	0.004	0.006
21423	England	2011/12	B	B	154	ST-41/44 complex	Blood	0.032	0.006	0.006	<0.002
21424	England	2011/12	B	B	9884	ST-213 complex	Blood	0.064	0.016	0.006	0.004
21425	England	2011/12	B	B	269	ST-269 complex	Blood	0.023	0.006	0.006	0.002
21426	England	2011/12	B	B	41	ST-41/44 complex	CSF	0.19	0.006	0.006	0.004
21427	England	2011/12	B	B	10290	UA	Blood	0.25	0.004	0.004	0.008
21428	England	2011/12	B	B	3496	ST-213 complex	Blood	0.125	0.006	0.006	0.006
21429	England	2011/12	B	B	4713	UA	CSF	0.064	0.008	0.008	0.004
21430	Northern Ireland	2011/12	C	C	10291	ST-269 complex	Blood	0.032	0.012	0.004	0.004
21431	England	2011/12	B	B	485	ST-41/44 complex	Blood	0.125	0.004	0.006	0.004
21432	England	2011/12	B	B	10292	ST-60 complex	Blood	0.023	0.002	0.008	0.002
21433	England	2011/12	B	B	1161	ST-269 complex	Blood	0.064	0.004	0.006	0.004
21434	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.023	0.016	0.006	0.003
21435	Wales	2011/12	B	B	2660	ST-213 complex	Blood	0.032	0.006	0.006	0.004
21436	England	2011/12	B	B	213	ST-213 complex	CSF	0.19	0.004	0.008	0.006
21437	England	2011/12	B	B	485	ST-41/44 complex	CSF	0.094	0.006	0.006	0.003
21438	England	2011/12	B	B	213	ST-213 complex	Blood	0.032	0.016	0.008	0.003
21439	Wales	2011/12	B	B	275	ST-269 complex	Blood	0.023	0.003	0.004	0.002
21440	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.125	0.004	0.006	0.006
21441	England	2011/12	B	B	749	ST-32 complex	CSF	0.19	0.003	0.006	0.004
21442	England	2011/12	B	B	9311	UA	Blood	0.047	0.016	0.006	0.003
21443	England	2011/12	Y	Y	1655	ST-23 complex	Joint	0.047	0.004	0.004	0.004
21444	England	2011/12	B	B	7143	UA	CSF	0.016	0.003	0.006	0.002
21445	Northern Ireland	2011/12	B	B	269	ST-269 complex	Blood	0.023	0.004	0.006	0.002
21447	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.016	0.004	0.006	<0.002
21448	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.032	0.003	0.006	0.003
21449	England	2011/12	B	B	269	ST-269 complex	Blood	0.023	0.008	0.006	0.002
21450	England	2011/12	B	B	340	ST-41/44 complex	Blood	0.064	0.004	0.006	0.003
21451	England	2011/12	Y	Y	6463	ST-23 complex	Blood	0.032	0.003	0.006	0.003
21452	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.023	0.004	0.004	0.002
21453	England	2011/12	B	B	2766	UA	Blood	0.032	0.006	0.004	0.004
21454	England	2011/12	W	W	1281	ST-22 complex	Blood	0.125	0.006	0.006	0.003
21455	England	2011/12	B	B	2203	ST-41/44 complex	Blood	0.032	0.008	0.006	0.002
21456	England	2011/12	B	B	213	ST-213 complex	Blood	0.064	0.047	0.004	0.003
21457	England	2011/12	B	B	213	ST-213 complex	CSF	0.047	0.047	0.006	0.003
21458	England	2011/12	C	C	11	ST-11 complex	Blood	0.047	0.008	0.008	0.004
21460	England	2011/12	B	B	571	ST-41/44 complex	CSF	0.047	0.094	0.006	0.002
21461	England	2011/12	B	B	7395	UA	Blood	0.19	0.006	0.004	0.004
21462	England	2011/12	B	B	34	ST-32 complex	Blood	0.094	0.006	0.004	0.004
21463	England	2011/12	B	B	3619	ST-41/44 complex	Blood	0.094	0.006	0.003	0.004
21464	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.023	0.006	0.004	<0.002
21465	England	2011/12	B	B	269	ST-269 complex	Blood	0.016	0.006	0.004	<0.002
21466	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.094	0.004	0.004	0.004
21467	England	2011/12	B	B	213	ST-213 complex	Blood	0.125	0.032	0.006	0.003
21468	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.19	0.006	0.003	0.002
21469	Northern Ireland	2011/12	B	B	639	ST-32 complex	Blood	0.047	0.012	0.006	0.003
21470	England	2011/12	B	B	10293	ST-41/44 complex	Blood	0.064	0.002	0.004	<0.002
21471	Wales	2011/12	B	B	1161	ST-269 complex	Blood	0.064	0.008	0.006	0.003
21472	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.047	0.003	0.004	0.002
21473	England	2011/12	Y	Y	10294	ST-23 complex	Blood	0.047	0.003	0.006	0.002
21474	England	2011/12	B	B	340	ST-41/44 complex	Blood	0.032	0.006	0.006	0.002
21475	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.064	0.003	0.004	0.003
21476	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.004
21477	England	2011/12	B	B	467	ST-269 complex	Blood	0.032	0.003	0.006	<0.002
21478	England	2011/12	B	B	571	ST-41/44 complex	CSF	0.064	0.003	0.004	0.003
21479	England	2011/12	B	B	3818	ST-41/44 complex	Blood	0.047	0.008	0.004	<0.002
21480	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.006	0.003
21481	England	2011/12	B	B	10295	ST-41/44 complex	Blood	0.047	0.012	0.006	0.002
21482	England	2011/12	B	B	10296	UA	CSF	0.032	0.006	0.004	<0.002
21483	England	2011/12	B	B	5849	UA	Blood	0.25	0.004	0.006	0.004
21484	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.023	0.002	0.004	<0.002

21485	Wales	2011/12	B	B	10297	UA	Blood	0.047	0.006	0.004	0.002
21486	England	2011/12	B	B	1195	ST-269 complex	Blood	0.032	0.008	0.004	<0.002
21487	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.125	0.006	0.004	0.004
21488	England	2011/12	B	B	2266	ST-41/44 complex	Blood	0.032	0.002	0.004	<0.002
21489	England	2011/12	B	B	269	ST-269 complex	Blood	0.032	0.004	0.004	<0.002
21490	England	2011/12	B	B	340	ST-41/44 complex	Blood	0.032	0.004	0.004	0.002
21493	England	2011/12	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	<0.002
21494	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.19	0.012	0.006	0.003
21495	England	2011/12	B	B	7460	ST-32 complex	Blood	0.19	0.006	0.004	0.003
21496	England	2011/12	B	B	1403	ST-41/44 complex	Blood	0.047	0.006	0.004	0.002
21497	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.064	0.003	0.004	0.003
21498	England	2011/12	C	C	467	ST-269 complex	Blood	0.047	0.008	0.008	0.003
21499	Wales	2011/12	W	W	11	ST-11 complex	Blood	0.064	0.012	0.006	0.003
21500	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.047	0.004	0.004	0.002
21501	England	2011/12	B	B	213	ST-213 complex	Blood	0.047	0.006	0.004	0.002
21502	England	2011/12	Y	Y	23	ST-23 complex	Blood	0.064	0.004	0.004	0.004
21503	England	2011/12	B	B	575	ST-213 complex	Blood	0.19	0.006	0.006	0.004
21504	England	2011/12	Y	Y	884	ST-167 complex	Blood	0.064	0.004	0.006	0.003
21505	England	2011/12	Y	Y	5987	ST-103 complex	Blood	0.125	0.016	0.006	0.003
21506	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.25	0.023	0.008	0.006
21507	England	2011/12	B	B	340	ST-41/44 complex	Blood	0.047	0.003	0.008	0.002
21508	England	2011/12	B	B	1163	ST-269 complex	Blood	0.047	0.003	0.004	0.004
26732	England	2013/14	C	C	11	ST-11 complex	Blood	0.25	0.016	0.004	0.012
27778	England	2012/13	B	B	1475	ST-41/44 complex	CSF	0.064	0.006	0.004	0.003
27779	England	2012/13	B	B	10692	ST-35 complex	Blood	0.064	0.003	0.006	0.003
27780	England	2012/13	B	B	213	ST-213 complex	Blood	0.047	0.023	0.004	0.003
27781	England	2012/13	B	B	9180	ST-269 complex	Blood	0.19	0.006	0.006	0.003
27782	England	2012/13	B	B	461	ST-461 complex	Blood	0.064	0.094	0.004	0.002
27783	England	2012/13	B	B	1097	ST-41/44 complex	CSF	0.047	0.004	0.004	0.002
27784	England	2012/13	B	B	4051	UA	Blood	0.094	0.032	0.004	0.003
27785	Wales	2012/13	B	B	1096	ST-32 complex	Blood	0.047	0.016	0.004	0.002
27786	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.19	0.008	0.006	0.003
27787	England	2012/13	B	B	1194	ST-41/44 complex	Blood	0.032	0.006	0.006	<0.002
27788	England	2012/13	B	B	154	ST-41/44 complex	Blood	0.19	0.002	0.004	0.003
27789	Wales	2012/13	B	B	1161	ST-269 complex	Blood	0.047	0.012	0.004	0.002
27790	England	2012/13	B	B	10693	ST-41/44 complex	Blood	0.047	0.002	0.004	<0.002
27791	England	2012/13	B	B	3695	ST-41/44 complex	Blood	0.094	0.008	0.006	0.002
27792	England	2012/13	B	B	42	ST-41/44 complex	Blood	0.094	0.004	0.008	0.004
27793	England	2012/13	B	B	1617	ST-22 complex	Blood	0.064	0.004	0.006	0.003
27794	England	2012/13	B	B	41	ST-41/44 complex	CSF	0.125	0.004	0.006	0.004
27795	England	2012/13	B	B	1194	ST-41/44 complex	Blood	0.047	0.003	0.006	0.002
27796	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.064	0.006	0.006	<0.002
27797	England	2012/13	B	B	10694	UA	Blood	0.064	0.003	0.004	0.002
27798	England	2012/13	B	B	1097	ST-41/44 complex	Blood	0.064	0.016	0.004	0.002
27799	England	2012/13	B	B	1161	ST-269 complex	Blood	0.094	0.023	0.004	0.003
27800	England	2012/13	B	B	10695	ST-269 complex	CSF	0.064	0.004	0.006	0.002
27801	Northern Ireland	2012/13	B	B	269	ST-269 complex	Blood	0.047	0.004	0.006	0.002
27802	England	2012/13	B	B	571	ST-41/44 complex	Blood	0.047	0.004	0.006	0.002
27803	England	2012/13	B	B	11	ST-11 complex	Blood	0.047	0.012	0.006	0.003
27804	England	2012/13	B	B	2157	ST-269 complex	Blood	0.047	0.012	0.004	0.003
27805	England	2012/13	B	B	9199	UA	CSF	0.19	0.003	0.004	0.006
27806	England	2012/13	B	B	3242	UA	CSF	0.064	0.004	0.006	0.003
27807	England	2012/13	B	B	1161	ST-269 complex	Blood	0.094	0.023	0.006	0.003
27808	England	2012/13	B	B	1161	ST-269 complex	Blood	0.125	0.016	0.006	0.003
27809	England	2012/13	B	B	290	ST-32 complex	Blood	0.125	0.012	0.006	0.004
27810	England	2012/13	B	B	1855	ST-269 complex	Blood	0.032	0.002	0.003	<0.002
27811	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.047	0.008	0.006	0.002
27812	England	2012/13	B	B	10696	ST-41/44 complex	CSF	0.032	0.006	0.006	<0.002
27813	England	2012/13	B	B	213	ST-213 complex	Blood	0.19	0.032	0.006	0.006
27814	England	2012/13	B	B	7261	ST-461 complex	Blood	0.25	0.032	0.006	0.004
27815	Wales	2012/13	B	B	10697	ST-213 complex	CSF	0.012	0.008	0.003	<0.002
27816	England	2012/13	B	B	10698	ST-41/44 complex	Joint	0.19	0.016	0.003	0.003
27817	England	2012/13	B	B	269	ST-269 complex	Blood	0.064	0.003	0.006	0.002
27818	England	2012/13	B	B	154	ST-41/44 complex	Blood	0.047	0.003	0.006	0.002
27819	England	2012/13	B	B	259	ST-32 complex	Blood	0.094	0.008	0.004	0.006
27820	England	2012/13	B	B	1163	ST-269 complex	CSF	0.19	0.004	0.004	0.003
27821	England	2012/13	B	B	1161	ST-269 complex	Blood	0.25	0.004	0.008	0.006
27822	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.064	0.003	0.006	0.003
27823	England	2012/13	B	B	7676	ST-213 complex	CSF	0.094	0.047	0.004	0.006
27824	England	2012/13	B	B	35	ST-35 complex	Blood	0.064	0.003	0.006	0.003
27825	England	2012/13	B	B	275	ST-269 complex	CSF	0.064	0.016	0.003	0.003
27826	England	2012/13	B	B	34	ST-32 complex	Blood	0.064	0.016	0.003	0.003
27827	Wales	2012/13	B	B	8049	ST-32 complex	Blood	0.25	0.004	0.004	0.004
27828	England	2012/13	B	B	10699	ST-213 complex	Blood	0.064	0.032	0.003	0.006
27829	England	2012/13	B	B	749	ST-32 complex	Blood	0.25	0.004	0.004	0.008
27830	England	2012/13	B	B	162	ST-162 complex	Blood	0.064	0.012	0.003	0.004
27831	England	2012/13	B	B	479	ST-269 complex	CSF	0.023	0.008	0.003	0.002
27832	England	2012/13	B	B	162	ST-162 complex	Blood	0.064	0.012	0.003	0.003
27833	England	2012/13	B	B	8054	ST-41/44 complex	CSF	0.047	0.004	0.002	0.003
27834	England	2012/13	B	B	1774	ST-269 complex	Blood	0.064	0.004	0.004	0.004
27835	England	2012/13	B	B	4713	UA	Blood	0.25	0.004	0.003	0.006
27836	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.125	0.003	0.002	0.003
27837	Northern Ireland	2012/13	B	B	154	ST-41/44 complex	Blood	0.064	0.003	0.003	0.002
27838	England	2012/13	B	B	10700	ST-32 complex	Blood	0.032	0.002	0.002	0.002
27839	England	2012/13	B	B	1946	ST-461 complex	Blood	0.5	0.023	0.002	0.004

27840	England	2012/13	B	B	2738	ST-269 complex	Blood	0.064	<0.002	0.002	0.006
27841	England	2012/13	B	B	1572	ST-1572 complex	Blood	0.25	0.008	0.002	0.008
27842	England	2012/13	B	B	1049	ST-269 complex	Blood	0.032	0.012	0.002	0.002
27843	England	2012/13	B	B	1946	ST-461 complex	Blood	0.25	0.002	0.002	0.004
27844	England	2012/13	B	B	275	ST-269 complex	Blood	0.047	0.002	0.002	0.002
27845	Wales	2012/13	B	B	213	ST-213 complex	Blood	0.032	0.008	0.003	0.002
27846	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.047	0.003	0.003	0.003
27847	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.047	0.003	0.003	0.003
27848	England	2012/13	B	B	1359	UA	Blood	0.023	0.012	0.002	0.002
27849	Wales	2012/13	B	B	1946	ST-461 complex	Blood	0.19	0.012	0.002	0.006
27850	England	2012/13	B	B	33	ST-32 complex	Blood	0.064	0.003	0.003	0.004
27851	England	2012/13	B	B	7789	ST-269 complex	Blood	0.064	0.004	0.002	0.003
27852	England	2012/13	B	B	10701	ST-35 complex	Blood	0.047	0.006	0.002	0.003
27853	England	2012/13	B	B	34	ST-32 complex	Blood	0.25	0.004	0.002	0.008
27854	England	2012/13	B	B	4953	ST-1572 complex	Blood	0.25	0.003	0.003	0.006
27855	Northern Ireland	2012/13	B	B	9774	ST-18 complex	Blood	0.047	0.008	0.003	0.004
27856	England	2012/13	B	B	10702	UA	Blood	0.125	0.002	0.004	0.006
27857	England	2012/13	B	B	282	ST-282 complex	CSF	0.047	0.008	0.003	0.003
27858	England	2012/13	B	B	8944	UA	Blood	0.047	0.004	0.003	0.006
27859	Northern Ireland	2012/13	B	B	269	ST-269 complex	Blood	0.047	0.006	0.003	0.002
27860	England	2012/13	B	B	479	ST-269 complex	Blood	0.064	0.003	0.003	0.003
27861	England	2012/13	B	B	10703	ST-269 complex	Blood	0.25	0.004	0.003	0.004
27862	England	2012/13	B	B	32	ST-32 complex	Blood	0.064	0.006	0.003	0.003
27863	England	2012/13	B	B	259	ST-32 complex	CSF	0.094	0.012	0.002	0.004
27864	England	2012/13	B	B	461	ST-461 complex	Blood	0.125	0.003	0.002	0.006
27865	England	2012/13	B	B	485	ST-41/44 complex	Blood	0.19	0.004	0.003	0.004
27866	England	2012/13	B	B	1161	ST-269 complex	Blood	0.125	0.008	0.003	0.003
27867	England	2012/13	B	B	1049	ST-269 complex	Blood	0.047	0.003	0.003	0.003
27868	England	2012/13	B	B	479	ST-269 complex	Blood	0.047	0.004	0.003	0.002
27869	England	2012/13	B	B	1161	ST-269 complex	CSF	0.094	0.002	0.003	0.004
27870	England	2012/13	B	B	1976	UA	Blood	0.032	0.004	0.003	0.002
27871	England	2012/13	B	B	8223	ST-461 complex	Blood	0.064	0.004	0.002	0.004
27872	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.19	0.008	0.002	0.008
27873	England	2012/13	B	B	3666	ST-41/44 complex	CSF	0.125	0.003	0.003	0.003
27874	England	2012/13	B	B	213	ST-213 complex	Blood	0.064	0.008	0.003	0.004
27875	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.032	0.006	0.003	0.002
27876	England	2012/13	B	B	1194	ST-41/44 complex	Blood	0.19	0.002	0.002	0.003
27877	England	2012/13	B	B	275	ST-269 complex	CSF	0.19	0.002	0.002	0.006
27878	England	2012/13	B	B	269	ST-269 complex	Blood	0.032	0.003	0.003	0.002
27879	England	2012/13	B	B	269	ST-269 complex	Blood	0.064	0.008	0.003	0.003
27880	England	2012/13	B	B	269	ST-269 complex	Blood	0.125	0.003	0.003	0.003
27881	England	2012/13	B	B	2123	UA	CSF	0.047	0.006	0.004	0.002
27882	England	2012/13	B	B	10704	ST-18 complex	CSF	0.094	0.006	0.002	0.008
27883	England	2012/13	B	B	213	ST-213 complex	Blood	0.047	0.094	0.002	0.003
27884	Wales	2012/13	B	B	479	ST-269 complex	Blood	0.032	0.003	0.003	0.002
27885	England	2012/13	B	B	1090	ST-41/44 complex	Blood	0.094	0.002	0.002	0.002
27886	England	2012/13	B	B	11142	UA	Blood	0.047	0.004	<0.002	0.003
27887	Wales	2012/13	B	B	10705	ST-461 complex	Blood	0.047	0.004	0.002	0.003
27888	England	2012/13	B	B	74	ST-32 complex	Blood	0.064	0.003	0.003	0.003
27889	England	2012/13	B	B	2821	ST-41/44 complex	Blood	0.047	0.006	0.002	0.003
27890	Wales	2012/13	B	B	1161	ST-269 complex	Blood	0.012	0.002	0.002	0.002
27891	England	2012/13	B	B	162	ST-162 complex	Blood	0.032	0.016	0.002	0.002
27892	England	2012/13	B	B	1161	ST-269 complex	Blood	0.25	0.004	0.002	0.004
27893	England	2012/13	B	B	269	ST-269 complex	Blood	0.023	0.003	0.002	0.002
27894	England	2012/13	B	B	32	ST-32 complex	Blood	0.047	0.032	0.003	0.003
27895	England	2012/13	B	B	1153	ST-41/44 complex	Blood	0.023	0.004	0.003	0.002
27896	England	2012/13	B	B	8288	ST-269 complex	Blood	0.016	0.004	0.003	0.002
27897	Wales	2012/13	B	B	1096	ST-32 complex	CSF	0.032	0.006	0.003	0.003
27898	England	2012/13	B	B	213	ST-213 complex	Blood	0.032	0.003	0.002	0.003
27899	Wales	2012/13	B	B	2592	ST-269 complex	Blood	0.016	0.002	0.003	0.002
27900	England	2012/13	B	B	10706	ST-41/44 complex	Blood	0.25	>32	0.003	0.012
27901	England	2012/13	B	B	1233	ST-41/44 complex	Blood	0.032	0.003	0.003	0.003
27903	England	2012/13	B	B	41	ST-41/44 complex	CSF	0.19	0.006	0.003	0.004
27904	England	2012/13	B	B	269	ST-269 complex	Blood	0.047	0.006	0.004	0.003
27905	England	2012/13	B	B	479	ST-269 complex	CSF	0.064	0.006	0.003	0.003
27906	England	2012/13	B	B	2166	ST-269 complex	Blood	0.047	0.004	0.003	0.002
27907	England	2012/13	B	B	461	ST-461 complex	Blood	0.19	0.006	0.003	0.006
27908	England	2012/13	B	B	1194	ST-41/44 complex	Blood	0.047	0.016	0.002	<0.002
27909	England	2012/13	B	B	2799	ST-41/44 complex	Blood	0.25	0.006	0.003	0.006
27910	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.19	0.004	0.003	0.004
27911	England	2012/13	B	B	1161	ST-269 complex	CSF	0.25	0.006	0.003	0.004
27912	Wales	2012/13	B	B	10707	ST-32 complex	Blood	0.25	0.004	0.003	0.004
27914	England	2012/13	B	B	461	ST-461 complex	Blood	0.19	0.008	0.002	0.004
27915	England	2012/13	B	B	35	ST-35 complex	Blood	0.064	0.004	0.002	0.003
27916	England	2012/13	B	B	213	ST-213 complex	Blood	0.032	0.016	0.002	0.002
27917	England	2012/13	B	B	10708	ST-269 complex	Blood	0.094	0.008	0.003	0.004
27918	England	2012/13	B	B	337	ST-41/44 complex	Blood	0.064	0.012	0.006	0.003
27919	England	2012/13	B	B	35	ST-35 complex	Blood	0.064	0.004	0.003	0.002
27920	England	2012/13	B	B	1161	ST-269 complex	Blood	0.125	0.006	0.003	0.004
27921	England	2012/13	B	B	10709	UA	Blood	0.094	0.006	0.003	0.003
27922	England	2012/13	B	B	479	ST-269 complex	Blood	0.047	0.006	0.003	0.002
27923	England	2012/13	B	B	479	ST-269 complex	Blood	0.032	0.006	0.003	0.002
27924	England	2012/13	B	B	10710	ST-41/44 complex	Blood	0.064	0.012	0.003	0.003
27925	England	2012/13	B	B	8006	UA	Blood	0.032	0.032	0.003	0.002
27926	England	2012/13	B	B	1195	ST-269 complex	Blood	0.032	0.006	0.003	0.002

27927	England	2012/13	B	B	1946	ST-461 complex	CSF	0.38	0.016	0.002	0.008
27928	England	2012/13	B	B	275	ST-269 complex	Blood	0.064	0.006	0.003	0.003
27929	England	2012/13	B	B	8054	ST-41/44 complex	Blood	0.064	0.006	0.003	0.003
27930	England	2012/13	B	B	1161	ST-269 complex	Blood	0.094	0.006	0.002	0.004
27931	England	2012/13	B	B	479	ST-269 complex	Blood	0.064	0.004	0.002	0.003
27932	England	2012/13	B	B	1774	ST-269 complex	Blood	0.064	0.008	0.003	0.002
27933	England	2012/13	B	B	5983	ST-461 complex	Blood	0.047	0.004	0.002	0.002
27934	England	2012/13	B	B	461	ST-461 complex	Blood	0.19	0.006	0.002	0.004
27935	England	2012/13	B	B	275	ST-269 complex	Blood	0.094	0.004	0.003	0.004
27936	England	2012/13	B	B	1161	ST-269 complex	Blood	0.064	0.125	0.004	0.002
27937	England	2012/13	B	B	269	ST-269 complex	CSF	0.032	0.003	0.003	<0.002
27938	England	2012/13	B	B	461	ST-461 complex	Blood	0.19	0.012	0.004	0.004
27939	England	2012/13	B	B	7196	UA	Blood	0.19	0.006	0.002	0.004
27940	England	2012/13	B	B	10711	UA	CSF	0.25	0.012	0.003	0.006
27941	England	2012/13	B	B	1946	ST-461 complex	Blood	0.19	0.003	0.002	0.002
27942	England	2012/13	B	B	9194	ST-213 complex	Blood	0.047	0.006	0.002	0.002
27943	England	2012/13	B	B	1475	ST-41/44 complex	Blood	0.064	0.064	0.003	0.002
27944	England	2012/13	B	B	40	ST-41/44 complex	Blood	0.047	0.003	0.003	0.002
27945	England	2012/13	B	B	1434	UA	Blood	0.38	0.012	0.003	0.016
27946	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.047	0.003	0.003	0.002
27947	England	2012/13	B	B	6761	ST-41/44 complex	Blood	0.064	0.003	0.004	0.003
27948	England	2012/13	B	B	162	ST-162 complex	Blood	0.047	0.004	0.003	0.002
27949	England	2012/13	B	B	1049	ST-269 complex	Blood	0.032	0.003	0.004	0.002
27950	Wales	2012/13	B	B	3893	ST-41/44 complex	CSF	0.125	0.008	0.004	0.003
27951	Wales	2012/13	B	B	1097	ST-41/44 complex	CSF	0.064	0.004	0.004	0.003
27952	England	2012/13	B	B	1572	ST-1572 complex	CSF	0.25	0.008	0.004	0.008
27953	England	2012/13	B	B	32	ST-32 complex	Blood	0.064	0.006	0.004	0.004
27954	England	2012/13	B	B	1194	ST-41/44 complex	Blood	0.064	0.002	0.004	0.002
27955	England	2012/13	B	B	269	ST-269 complex	Blood	0.047	0.003	0.004	0.002
27956	England	2012/13	B	B	1194	ST-41/44 complex	Blood	0.064	0.004	0.004	0.002
27957	England	2012/13	B	B	34	ST-32 complex	Blood	0.032	0.032	0.003	0.002
27958	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.047	0.004	0.004	0.003
27959	England	2012/13	B	B	1161	ST-269 complex	BONE MARROW	0.125	0.006	0.003	0.006
27960	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.047	0.004	0.004	0.003
27961	England	2012/13	B	B	1161	ST-269 complex	CSF	0.094	0.004	0.004	0.004
27962	England	2012/13	B	B	1802	ST-282 complex	Blood	0.047	0.003	0.004	0.002
27963	England	2012/13	B	B	213	ST-213 complex	Blood	0.19	0.006	0.004	0.004
27964	England	2012/13	B	B	749	ST-32 complex	Blood	0.38	0.012	0.004	0.008
27965	England	2012/13	B	B	213	ST-213 complex	Blood	0.064	0.004	0.004	0.002
27966	England	2012/13	B	B	1194	ST-41/44 complex	Blood	0.064	0.004	0.004	0.004
27967	England	2012/13	B	B	1770	ST-41/44 complex	CSF	0.094	0.006	0.004	0.004
27968	England	2012/13	B	B	9293	ST-162 complex	Blood	0.19	0.004	0.004	0.004
27969	England	2012/13	B	B	282	ST-282 complex	Blood	0.094	0.006	0.006	0.003
27970	England	2012/13	B	B	10712	ST-269 complex	Blood	0.19	0.004	0.004	0.002
27971	Northern Ireland	2012/13	B	B	10713	UA	Blood	0.064	0.008	0.004	0.004
27972	England	2012/13	B	B	10714	UA	CSF	0.064	0.004	0.004	0.003
27973	England	2012/13	B	B	9327	ST-60 complex	Blood	0.047	0.004	0.004	0.003
27974	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.047	0.004	0.004	0.002
27975	Wales	2012/13	B	B	269	ST-269 complex	Blood	0.047	0.004	0.006	0.003
27976	England	2012/13	B	B	35	ST-35 complex	Blood	0.047	0.012	0.004	0.002
27977	England	2012/13	B	B	269	ST-269 complex	Blood	0.016	0.006	0.003	0.002
27978	England	2012/13	B	B	1194	ST-41/44 complex	Blood	0.064	0.004	0.004	0.003
27979	England	2012/13	B	B	269	ST-269 complex	Blood	0.032	0.004	0.004	0.002
27980	England	2012/13	B	B	575	ST-213 complex	Blood	0.19	0.006	0.002	0.003
27981	England	2012/13	B	B	5357	ST-41/44 complex	Blood	0.064	0.003	0.004	0.003
27982	England	2012/13	B	B	275	ST-269 complex	Blood	0.094	0.003	0.004	0.002
27983	England	2012/13	B	B	4256	ST-41/44 complex	CSF	0.032	0.003	0.006	0.003
27984	England	2012/13	B	B	2203	ST-41/44 complex	Blood	0.064	0.003	0.003	0.004
27985	England	2012/13	B	B	10535	ST-41/44 complex	Joint	0.064	0.003	0.004	0.004
27986	England	2012/13	B	B	41	ST-41/44 complex	CSF	0.064	0.003	0.002	0.003
27987	England	2012/13	B	B	5151	UA	Blood	0.19	0.004	0.003	0.008
27988	England	2012/13	B	B	213	ST-213 complex	Blood	0.047	0.008	0.002	0.004
27989	England	2012/13	B	B	1163	ST-269 complex	Blood	0.19	0.003	0.002	0.008
27990	England	2012/13	B	B	275	ST-269 complex	Blood	0.19	0.008	0.003	0.008
27991	England	2012/13	B	B	9829	ST-269 complex	CSF	0.023	0.002	0.002	0.002
27992	Wales	2012/13	B	B	11	ST-11 complex	CSF	0.047	0.016	0.002	0.004
27993	England	2012/13	B	B	7143	UA	Blood	0.032	0.003	0.003	0.003
27994	England	2012/13	B	B	1194	ST-41/44 complex	Blood	0.047	0.003	0.003	0.003
27995	England	2012/13	B	B	485	ST-41/44 complex	Blood	0.25	0.012	0.003	0.004
27996	England	2012/13	B	B	207	ST-41/44 complex	Blood	0.032	0.004	0.002	0.002
27997	Wales	2012/13	B	B	1161	ST-269 complex	Blood	0.25	0.003	0.003	0.006
27998	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.19	0.006	0.002	0.006
27999	England	2012/13	B	B	5849	UA	CSF	0.25	0.003	0.003	0.008
28000	England	2012/13	B	B	3101	ST-41/44 complex	Blood	0.064	0.003	0.003	0.004
28001	Northern Ireland	2012/13	B	B	275	ST-269 complex	Blood	0.023	0.004	0.003	0.002
28002	Wales	2012/13	B	B	8049	ST-32 complex	Blood	0.19	0.003	0.002	0.004
28003	England	2012/13	B	B	1194	ST-41/44 complex	Blood	0.125	0.004	0.002	0.004
28004	Wales	2012/13	B	B	10715	UA	Blood	0.064	0.032	0.003	0.004
28005	Wales	2012/13	B	B	1161	ST-269 complex	Blood	0.047	0.004	0.002	0.003
28006	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.094	0.003	0.002	0.004
28007	Wales	2012/13	B	B	1096	ST-32 complex	Blood	0.047	0.006	0.003	0.004
28009	Wales	2012/13	B	B	8539	ST-41/44 complex	Blood	0.047	0.004	0.003	0.003
28010	England	2012/13	B	B	213	ST-213 complex	Blood	0.094	0.008	0.002	0.004
28011	England	2012/13	B	B	275	ST-269 complex	Blood	0.064	0.002	0.003	0.004
28012	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.032	0.003	0.002	0.002

28013	Wales	2012/13	B	B	41	ST-41/44 complex	Blood	0.19	0.047	0.003	0.006
28014	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.125	0.012	0.002	0.004
28015	Northern Ireland	2012/13	B	B	41	ST-41/44 complex	Blood	0.047	0.016	0.003	0.002
28016	England	2012/13	B	B	269	ST-269 complex	Blood	0.032	0.003	0.002	0.002
28017	England	2012/13	B	B	1946	ST-461 complex	Blood	0.125	0.047	0.002	0.006
28019	England	2012/13	B	B	840	ST-167 complex	Blood	0.064	0.008	0.002	0.004
28020	England	2012/13	B	B	1161	ST-269 complex	Blood	0.094	0.008	0.003	0.008
28021	England	2012/13	B	B	1163	ST-269 complex	Blood	0.19	0.016	0.002	0.008
28022	England	2012/13	B	B	1273	ST-269 complex	Blood	0.047	0.002	0.002	0.004
28023	England	2012/13	B	B	10338	ST-213 complex	Blood	0.064	0.008	0.002	0.006
28024	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.032	0.004	0.002	0.004
28025	England	2012/13	B	B	10717	ST-32 complex	Blood	0.047	0.004	0.002	0.006
28026	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.19	0.006	0.002	0.008
28027	England	2012/13	B	B	1157	ST-1157 complex	CSF	0.047	0.006	0.002	0.006
28028	England	2012/13	B	B	10718	ST-41/44 complex	Blood	0.125	0.023	0.008	0.008
28029	England	2012/13	B	B	162	ST-162 complex	Blood	0.064	0.008	0.004	0.006
28030	England	2012/13	B	B	1194	ST-41/44 complex	Blood	0.064	0.004	0.004	0.004
28031	England	2012/13	B	B	1049	ST-269 complex	Blood	0.064	0.008	0.004	0.006
28032	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.047	0.004	0.004	0.004
28033	England	2012/13	B	B	1823	ST-41/44 complex	Blood	0.125	0.004	0.006	0.008
28034	England	2012/13	B	B	10719	ST-213 complex	Blood	0.064	0.012	0.006	0.004
28035	England	2012/13	B	B	10720	ST-269 complex	Blood	0.032	0.003	0.004	0.003
28036	England	2012/13	B	B	5330	UA	Joint	0.047	0.023	0.004	0.004
28037	England	2012/13	B	B	6791	ST-269 complex	Blood	0.047	0.004	0.006	0.004
28038	England	2012/13	B	B	32	ST-32 complex	CSF	0.094	0.016	0.006	0.004
28039	England	2012/13	B	B	8176	ST-41/44 complex	Blood	0.064	0.008	0.006	0.003
28040	England	2012/13	B	B	1159	UA	Blood	0.064	0.006	0.006	0.006
28041	England	2012/13	B	B	1575	UA	Blood	0.064	0.004	0.004	0.004
28042	England	2012/13	B	B	269	ST-269 complex	Blood	0.047	0.006	0.006	0.003
28043	England	2012/13	B	B	1946	ST-461 complex	Blood	0.38	0.006	0.004	0.008
28044	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.004	0.006
28045	Wales	2012/13	B	B	283	ST-269 complex	Blood	0.047	0.004	0.004	0.003
28046	England	2012/13	B	B	10721	ST-41/44 complex	Blood	0.125	0.003	0.004	0.006
28047	England	2012/13	B	B	162	ST-162 complex	Blood	0.064	0.006	0.006	0.004
28048	England	2012/13	B	B	1430	ST-60 complex	Blood	0.047	0.006	0.004	0.004
28049	England	2012/13	B	B	46	ST-41/44 complex	Blood	0.064	0.006	0.006	0.004
28050	England	2012/13	B	B	1049	ST-269 complex	Blood	0.047	0.004	0.004	0.003
28051	England	2012/13	B	B	1163	ST-269 complex	Blood	0.19	0.003	0.004	0.008
28052	England	2012/13	B	B	10722	UA	Blood	0.047	0.004	0.004	0.004
28053	England	2012/13	B	B	5849	UA	Blood	0.064	0.004	0.004	0.004
28054	Wales	2012/13	B	B	213	ST-213 complex	Blood	0.064	0.004	0.006	0.006
28055	England	2012/13	B	B	275	ST-269 complex	Blood	0.064	0.008	0.008	0.004
28056	England	2012/13	B	B	269	ST-269 complex	Blood	0.047	0.004	0.006	0.003
28057	England	2012/13	B	B	254	ST-254 complex	Blood	0.064	0.006	0.004	0.006
28058	England	2012/13	B	B	213	ST-213 complex	Blood	0.094	0.016	0.004	0.006
28059	England	2012/13	B	B	7955	ST-41/44 complex	Blood	0.064	0.006	0.004	0.004
28060	England	2012/13	B	B	103	ST-103 complex	Blood	0.032	0.004	0.003	0.004
28061	England	2012/13	B	B	154	ST-41/44 complex	Blood	0.032	0.006	0.004	0.006
28063	England	2012/13	B	B	3120	ST-213 complex	Blood	0.19	0.023	0.008	0.004
28064	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.19	0.004	0.008	0.004
28065	England	2012/13	B	B	269	ST-269 complex	Blood	0.047	0.004	0.003	0.008
28066	England	2012/13	B	B	275	ST-269 complex	Blood	0.064	0.008	0.008	0.004
28067	England	2012/13	B	B	103	ST-103 complex	Blood	0.032	0.006	0.006	0.002
28068	England	2012/13	B	B	1159	UA	Blood	0.125	0.047	0.008	0.012
28069	England	2012/13	B	B	1161	ST-269 complex	Blood	0.064	0.008	0.004	0.006
28070	England	2012/13	B	B	275	ST-269 complex	Blood	0.032	0.004	0.006	0.003
28071	England	2012/13	B	B	162	ST-162 complex	Blood	0.25	0.004	0.006	0.008
28072	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.064	0.006	0.006	0.004
28073	England	2012/13	B	B	2080	ST-41/44 complex	Blood	0.094	0.006	0.008	0.008
28074	England	2012/13	B	B	1161	ST-269 complex	Blood	0.012	0.006	0.006	0.004
28075	England	2012/13	B	B	1161	ST-269 complex	Blood	0.094	0.032	0.006	0.004
28076	England	2012/13	B	B	41	ST-41/44 complex	Blood	0.094	0.008	0.004	0.006
28077	England	2012/13	B	B	10723	ST-213 complex	Blood	0.047	0.016	0.006	0.004
28078	England	2012/13	B	B	10724	ST-269 complex	Blood	0.19	0.008	0.006	0.004
28079	England	2012/13	C	C	5133	ST-103 complex	Blood	0.016	0.008	0.004	<0.002
28080	England	2012/13	C	C	11	ST-11 complex	CSF	0.047	0.004	0.008	<0.002
28081	England	2012/13	C	C	467	ST-269 complex	Blood	0.047	0.004	0.006	0.002
28082	England	2012/13	C	C	11	ST-11 complex	Blood	0.25	0.125	0.006	0.004
28083	England	2012/13	C	C	11	ST-11 complex	Blood	0.25	0.016	0.006	0.006
28084	England	2012/13	C	C	11	ST-11 complex	Blood	0.094	0.004	0.008	0.004
28085	England	2012/13	C	C	11	ST-11 complex	Blood	0.094	0.032	0.003	0.004
28086	England	2012/13	C	C	1466	ST-174 complex	Blood	0.094	0.012	<0.002	0.004
28087	England	2012/13	C	C	1466	ST-174 complex	Blood	0.125	0.012	<0.002	0.004
28088	England	2012/13	C	C	9777	UA	Blood	0.032	0.012	<0.002	0.002
28089	England	2012/13	C	C	11	ST-11 complex	Blood	0.094	0.012	0.003	0.004
28090	England	2012/13	C	C	11	ST-11 complex	Joint	0.047	0.016	0.003	0.004
28091	Northern Ireland	2012/13	C	C	467	ST-269 complex	Blood	0.064	0.006	0.003	0.004
28092	England	2012/13	C	C	11	ST-11 complex	Blood	0.125	0.008	0.004	0.006
28093	England	2012/13	C	C	11	ST-11 complex	Blood	0.25	0.012	0.004	0.008
28094	England	2012/13	C	C	11	ST-11 complex	Blood	0.25	0.012	0.006	0.006
28095	England	2012/13	C	C	11	ST-11 complex	Blood	0.19	0.023	0.003	0.008
28096	England	2012/13	C	C	5315	UA	Blood	0.004	0.016	<0.002	<0.002
28097	England	2012/13	C	C	11	ST-11 complex	Blood	0.19	0.003	0.003	0.004
28098	England	2012/13	C	C	11	ST-11 complex	Blood	0.19	0.023	0.004	0.008
28099	England	2012/13	C	C	11	ST-11 complex	Blood	0.19	0.012	0.004	0.012

28100	England	2012/13	C	C	11	ST-11 complex	Blood	0.19	0.008	0.004	0.012
28101	England	2012/13	C	C	5133	ST-103 complex	Blood	0.125	0.006	0.004	0.002
28102	England	2012/13	C	C	11	ST-11 complex	Blood	0.094	0.006	0.006	0.006
28103	England	2012/13	C	C	11	ST-11 complex	Blood	0.25	0.012	0.004	0.008
28104	England	2012/13	C	C	11	ST-11 complex	Blood	0.25	0.016	0.006	0.008
28105	England	2012/13	C	C	11	ST-11 complex	Blood	0.25	0.016	0.004	0.008
28106	England	2012/13	C	C	11	ST-11 complex	Blood	0.047	0.004	0.008	0.004
28107	England	2012/13	NG	E	10301	ST-1157 complex	Blood	0.047	0.006	0.008	0.002
28109	England	2012/13	NG	CNL	823	ST-198 complex	Blood	0.25	0.125	0.006	0.008
28111	England	2012/13	NG	B	213	ST-213 complex	Blood	0.125	0.003	0.003	0.004
28112	England	2012/13	NG	B	41	ST-41/44 complex	Blood	0.19	0.004	0.004	0.006
28113	England	2012/13	NG	E	1157	ST-1157 complex	Blood	0.032	0.016	0.003	0.003
28118	England	2012/13	W	W	184	ST-22 complex	Blood	0.094	0.006	0.008	0.003
28120	England	2012/13	W	W	1286	ST-22 complex	Blood	0.19	0.012	0.003	0.003
28121	Wales	2012/13	W	W	10651	ST-11 complex	Blood	0.047	0.004	0.003	0.003
28123	England	2012/13	W	W	184	ST-22 complex	Blood	0.125	0.006	0.004	0.004
28124	England	2012/13	W	W	22	ST-22 complex	Blood	0.125	0.002	0.003	0.004
28126	Wales	2012/13	W	W	184	ST-22 complex	CSF	0.125	0.016	0.003	0.003
28127	England	2012/13	W	W	1286	ST-22 complex	Blood	0.125	0.004	0.004	0.003
28129	England	2012/13	W	W	1281	ST-22 complex	Blood	0.125	0.006	0.002	0.002
28130	England	2012/13	W/Y	W/Y	1655	ST-23 complex	Blood	0.047	0.004	0.002	0.003
28133	England	2012/13	W	W	1286	ST-22 complex	CSF	0.19	0.008	0.003	0.003
28140	England	2012/13	W	W	184	ST-22 complex	Blood	0.19	0.008	0.006	0.003
28145	England	2012/13	W	W	22	ST-22 complex	Blood	0.25	0.008	0.008	0.004
28148	Wales	2012/13	W	W	10651	ST-11 complex	Blood	0.064	0.008	0.003	0.004
28155	England	2012/13	W	W	10726	ST-22 complex	Joint	0.19	0.094	0.004	0.004
28159	Northern Ireland	2012/13	W	W	11	ST-11 complex	Blood	0.094	0.008	0.008	0.004
28160	England	2012/13	W	W	184	ST-22 complex	Blood	0.094	0.012	0.008	0.003
28165	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.064	0.004	0.006	0.003
28166	Northern Ireland	2012/13	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.006	0.003
28167	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
28168	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.004	0.003
28170	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.094	0.016	0.006	0.003
28171	Wales	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.006	0.002
28172	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.047	<0.002	0.004	0.006
28173	England	2012/13	Y	Y	1466	ST-174 complex	Blood	0.094	0.006	0.003	0.006
28174	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.19	0.003	0.003	0.004
28175	England	2012/13	Y	Y	3030	ST-23 complex	Blood	0.19	0.002	<0.002	0.003
28176	England	2012/13	Y	Y	103	ST-103 complex	Blood	0.023	0.003	0.004	0.002
28177	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.19	0.002	0.002	0.006
28178	England	2012/13	Y	Y	1655	ST-23 complex	Joint	0.094	0.004	0.002	0.008
28179	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.002	0.002	0.003
28180	England	2012/13	Y	Y	1466	ST-174 complex	Joint	0.5	0.008	0.002	0.016
28181	England	2012/13	Y	Y	10294	ST-23 complex	Joint	0.064	0.003	0.003	0.003
28182	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.002	0.003
28183	England	2012/13	Y	Y	10727	ST-167 complex	Blood	0.032	0.006	0.002	0.003
28184	England	2012/13	Y	Y	10728	ST-167 complex	Blood	0.19	0.003	0.002	0.012
28185	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.125	0.002	0.002	0.003
28186	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.064	0.002	0.002	0.003
28187	England	2012/13	Y	Y	114	ST-22 complex	Blood	0.094	0.003	0.003	0.008
28188	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.125	0.003	0.002	0.004
28189	England	2012/13	Y	Y	10729	ST-167 complex	Blood	0.032	0.002	0.002	0.003
28190	England	2012/13	Y	Y	23	ST-23 complex	Joint	0.047	0.003	0.002	0.003
28191	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.064	0.003	0.002	0.003
28192	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.002	0.003
28193	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.002	0.004
28194	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.125	0.002	0.002	0.004
28195	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.064	0.006	0.002	0.004
28196	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.002	0.003
28197	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.125	0.004	0.002	0.006
28198	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.094	0.003	0.003	0.004
28199	England	2012/13	Y	Y	114	ST-22 complex	Blood	0.064	0.003	0.004	0.003
28200	England	2012/13	Y	Y	1655	ST-23 complex	CSF	0.064	0.006	0.003	0.006
28201	Northern Ireland	2012/13	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.002	0.004
28202	England	2012/13	Y	Y	10730	ST-167 complex	Blood	0.064	0.004	0.002	0.003
28203	England	2012/13	Y	Y	114	ST-22 complex	Blood	0.064	0.003	0.003	0.006
28204	England	2012/13	Y	Y	10728	ST-167 complex	Blood	0.19	0.002	0.002	0.016
28205	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.003	0.002
28206	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.032	0.003	0.003	0.002
28207	England	2012/13	Y	Y	1655	ST-23 complex	BRAIN	0.012	0.003	0.002	0.002
28208	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.004	0.003
28209	England	2012/13	Y	Y	1655	ST-23 complex	CSF	0.064	0.004	0.003	0.003
28210	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.125	0.004	0.004	0.006
28211	Northern Ireland	2012/13	Y	Y	3980	ST-167 complex	Blood	0.5	0.006	0.004	0.016
28212	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.064	0.004	0.004	0.004
28213	England	2012/13	Y	Y	168	ST-167 complex	Blood	0.094	0.003	0.004	0.006
28214	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.023	0.002	0.002	0.002
28215	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.002
28216	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.012	0.003	0.002	0.002
28217	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.002	0.003	0.004
28218	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.002	0.006
28219	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.002	0.006
28220	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.002	0.002	0.002
28221	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.002	0.004
28222	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.032	0.003	0.002	0.003

28223	England	2012/13	Y	Y	1655	ST-23 complex	CSF	0.032	0.004	0.002	0.002
28224	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.003	0.004
28225	England	2012/13	Y	Y	3015	UA	Blood	0.047	0.012	0.002	0.006
28226	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.125	0.003	0.002	0.004
28227	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.032	0.003	0.002	0.003
28228	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.032	0.006	0.004	0.004
28229	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.002	0.004
28230	England	2012/13	Y	Y	10732	ST-23 complex	Blood	0.047	0.004	0.002	0.004
28231	England	2012/13	Y	Y	23	ST-23 complex	Blood	0.094	0.004	0.004	0.008
28232	England	2012/13	Y	Y	3342	ST-865 complex	Blood	0.016	0.032	0.004	0.002
28233	England	2012/13	Y	Y	4446	ST-23 complex	Blood	0.094	0.003	0.006	0.006
28234	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.004
28235	England	2012/13	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.004
29727	Wales	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.003	0.006	0.004
29895	Northern Ireland	2013/14	C	C	11	ST-11 complex	Blood	0.094	0.006	0.008	0.008
29897	England	2013/14	C	C	11	ST-11 complex	Blood	0.064	0.012	0.008	0.004
29898	England	2013/14	C	C	11	ST-11 complex	Blood	0.094	0.006	0.008	0.004
30149	England	2013/14	W	W	1617	ST-22 complex	Blood	0.032	0.006	0.008	0.003
30169	Northern Ireland	2013/14	W	W	11	ST-11 complex	CSF	0.094	0.008	0.008	0.006
30210	England	2013/14	C	C	11	ST-11 complex	Blood	0.38	0.047	0.012	0.016
30211	England	2013/14	Y	Y	23	ST-23 complex	Blood	0.047	0.004	0.004	0.004
30212	England	2013/14	C	C	NK	INCOMPLETE MLST	CSF	0.25	0.125	0.008	0.012
30213	England	2013/14	C	C	NK	INCOMPLETE MLST	Blood	0.25	0.016	0.008	0.008
30214	England	2013/14	C	C	11	ST-11 complex	Blood	0.125	0.032	0.008	0.012
30215	England	2013/14	C	C	11	ST-11 complex	Blood	0.064	0.023	0.008	0.008
31162	England	2013/14	B	B	11	ST-11 complex	Blood	0.094	0.125	0.006	0.008
31163	England	2014/15	B	B	485	ST-41/44 complex	Blood	0.125	0.012	0.006	0.006
34502	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.094	0.004	0.006	0.004
34503	England	2013/14	Y	NK	1655	ST-23 complex	Blood	0.032	0.003	0.006	0.004
34504	England	2013/14	B	B	269	ST-269 complex	Blood	0.047	0.002	0.006	0.002
34505	England	2013/14	B	B	343	ST-32 complex	Blood	0.38	0.008	0.008	0.023
34506	England	2013/14	B	B	5972	ST-269 complex	Blood	0.064	0.003	0.006	0.006
34507	England	2013/14	B	B	41	ST-41/44 complex	Joint	0.125	0.016	0.004	0.004
34508	England	2013/14	B	B	1423	ST-41/44 complex	Blood	0.094	0.006	0.008	0.006
34509	Wales	2013/14	B	B	1855	ST-269 complex	Blood	0.047	0.002	0.006	0.003
34510	England	2013/14	B	B	1194	ST-41/44 complex	Blood	0.064	0.023	0.004	0.002
34511	England	2013/14	B	B	32	ST-32 complex	Blood	0.125	0.008	0.008	0.008
34512	England	2013/14	W	NK	184	ST-22 complex	Blood	0.047	0.004	0.006	0.003
34513	England	2013/14	B	B	9126	ST-174 complex	Blood	0.094	0.003	0.006	0.006
34514	England	2013/14	B	B	1214	ST-269 complex	Blood	0.047	0.016	0.006	0.003
34515	England	2013/14	B	B	749	ST-32 complex	Blood	0.19	0.003	0.006	0.008
34516	England	2013/14	B	B	213	ST-213 complex	Blood	0.023	0.012	0.008	0.002
34517	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.19	0.004	0.004	0.008
35422	England	2013/14	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.016	0.004	0.016
35423	England	2013/14	W	W	184	ST-22 complex	Blood	0.125	0.023	0.006	0.004
35424	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.003	0.006
35426	England	2013/14	B	B	11225	ST-41/44 complex	Blood	0.064	0.016	0.006	0.006
35427	England	2013/14	B	B	1946	ST-461 complex	Blood	0.38	0.19	0.006	0.008
35428	England	2013/14	B	B	34	ST-32 complex	Blood	0.19	0.004	0.004	0.012
35429	England	2013/14	B	B	1163	ST-269 complex	CSF	0.047	0.003	0.006	0.006
35430	England	2013/14	B	B	275	ST-269 complex	Blood	0.064	0.004	0.006	0.006
35431	Northern Ireland	2013/14	B	B	11226	ST-213 complex	Blood	0.032	0.002	0.004	0.003
35432	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.19	0.006	0.008	0.023
35434	England	2013/14	B	B	303	ST-41/44 complex	Blood	0.25	0.008	0.004	0.012
35435	England	2013/14	Y	Y	1655	ST-23 complex	Joint	0.047	0.004	0.004	0.004
35436	England	2013/14	B	B	461	ST-461 complex	Blood	0.125	0.012	0.004	0.008
35437	England	2013/14	B	B	7516	ST-41/44 complex	Blood	0.023	0.006	0.004	0.008
35438	England	2013/14	B	B	11227	ST-41/44 complex	Blood	0.125	0.003	0.004	0.008
35439	England	2013/14	B	B	1163	ST-269 complex	Blood	0.19	0.002	0.006	0.008
35440	England	2013/14	B	B	11229	ST-41/44 complex	Blood	0.047	0.003	0.004	0.003
35441	England	2013/14	B	B	283	ST-269 complex	Blood	0.047	0.012	0.006	0.003
35442	Wales	2013/14	B	B	213	ST-213 complex	Blood	0.094	0.008	0.006	0.006
35443	England	2013/14	B	B	269	ST-269 complex	Blood	0.032	0.004	0.006	0.003
35444	England	2013/14	B	B	11237	ST-269 complex	Blood	0.023	0.008	0.003	0.003
35445	England	2013/14	Y	Y	9842	ST-23 complex	Blood	0.064	0.006	0.004	0.006
35446	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.004	0.006
35447	England	2013/14	B	B	11238	ST-269 complex	Blood	0.047	0.003	0.004	0.003
35448	England	2013/14	B	B	1946	ST-461 complex	CSF	0.5	0.004	0.004	0.008
35449	England	2013/14	W/Y	W/Y	1624	ST-167 complex	Blood	0.25	0.006	0.004	0.016
35450	England	2013/14	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.006	0.004	0.004
35451	Wales	2013/14	B	B	11239	ST-269 complex	Blood	0.25	0.012	0.006	0.008
35452	England	2013/14	B	B	162	ST-162 complex	CSF	0.38	0.012	0.006	0.008
35453	England	2013/14	W	W	184	ST-22 complex	Blood	0.094	0.016	0.006	0.003
35454	England	2013/14	B	B	269	ST-269 complex	Blood	0.047	0.006	0.006	0.003
35456	Northern Ireland	2013/14	Y	Y	23	ST-23 complex	Blood	0.047	0.006	0.006	0.004
35457	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.004	0.006
35458	Wales	2013/14	B	B	11328	UA	Blood	0.064	0.023	0.004	0.004
35459	England	2013/14	B	B	2821	ST-41/44 complex	CSF	0.064	0.008	0.004	0.004
35460	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.047	0.008	0.004	0.004
35461	England	2013/14	B	B	1163	ST-269 complex	Blood	0.19	0.003	0.004	0.006
35462	England	2013/14	B	B	2314	ST-41/44 complex	Blood	0.094	0.006	0.004	0.008
35463	England	2013/14	B	B	10868	ST-41/44 complex	Blood	0.023	0.002	0.004	0.002
35464	Wales	2013/14	B	B	NK	INCOMPLETE MLST	CSF	0.125	0.006	0.004	0.006
35465	England	2013/14	B	B	NK	INCOMPLETE MLST	Blood	0.047	0.023	0.006	0.004
35466	England	2013/14	B	B	213	ST-213 complex	Blood	0.125	0.094	0.006	0.008

35467	England	2013/14	B	B	1194	ST-41/44 complex	Blood	0.047	0.006	0.004	0.004
35468	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.25	0.004	0.004	0.008
35469	England	2013/14	B	B	35	ST-35 complex	Blood	0.064	0.008	0.006	0.003
35470	England	2013/14	B	B	8380	ST-41/44 complex	Blood	0.125	0.003	0.004	0.006
35471	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.19	0.004	0.006	0.006
35472	England	2013/14	Y	Y	1624	ST-167 complex	Blood	0.125	0.004	0.006	0.012
35473	Wales	2013/14	B	B	11243	UA	Joint	0.064	0.016	0.004	0.004
35474	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.094	0.016	0.006	0.008
35475	England	2013/14	B	B	11329	UA	CSF	0.19	0.003	0.008	0.008
35477	England	2013/14	B	B	9180	ST-269 complex	Blood	0.125	0.004	0.004	0.006
35478	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.19	0.008	0.006	0.006
35480	England	2013/14	B	B	461	ST-461 complex	CSF	0.25	0.004	0.006	0.008
35481	England	2013/14	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.002	0.006	0.006
35482	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.047	0.008	0.006	0.003
35483	England	2013/14	B	B	485	ST-41/44 complex	Blood	0.19	0.006	0.008	0.006
35484	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.006	0.006
35485	England	2013/14	B	B	1161	ST-269 complex	Joint	0.25	0.008	0.006	0.004
35487	England	2013/14	Y	Y	1655	ST-23 complex	Pericardium	0.064	0.002	0.004	0.004
35488	England	2013/14	B	B	213	ST-213 complex	Blood	0.047	0.016	0.006	0.004
35489	England	2013/14	B	B	485	ST-41/44 complex	Blood	0.19	0.008	0.006	0.006
35491	England	2013/14	Y	Y	23	ST-23 complex	Blood	0.064	0.003	0.006	0.003
35492	England	2013/14	B	B	1475	ST-41/44 complex	Blood	0.047	0.016	0.008	0.004
35493	England	2013/14	B	B	11245	UA	Blood	0.047	0.004	0.006	0.004
35494	England	2013/14	B	B	8004	ST-269 complex	Blood	0.032	0.004	0.006	0.003
35495	England	2013/14	B	B	11246	ST-269 complex	Blood	0.094	0.023	0.012	0.006
35496	England	2013/14	B	B	NK	INCOMPLETE MLST	Blood	0.064	0.008	0.006	0.004
35497	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.125	0.004	0.008	0.008
35498	England	2013/14	B	B	32	ST-32 complex	Blood	0.064	0.008	0.006	0.004
35499	England	2013/14	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.004	0.006	0.006
35500	England	2013/14	B	B	11	ST-11 complex	Blood	0.064	0.016	0.008	0.006
35501	England	2013/14	Y	Y	1627	ST-167 complex	Joint	0.064	0.004	0.006	0.008
35502	England	2013/14	B	B	11	ST-11 complex	Blood	0.064	0.016	0.008	0.008
35503	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.25	0.006	0.008	0.008
35504	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.064	0.012	0.008	0.004
35505	England	2013/14	B	B	35	ST-35 complex	Blood	0.25	0.008	0.008	0.008
35506	England	2013/14	B	B	269	ST-269 complex	CSF	0.047	0.032	0.008	0.004
35508	England	2013/14	Y	Y	23	ST-23 complex	Blood	0.094	0.006	0.008	0.008
35509	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.064	0.032	0.006	0.004
35510	England	2013/14	B	B	136	ST-41/44 complex	CSF	0.032	0.012	0.006	0.003
35511	England	2013/14	B	B	60	ST-60 complex	Blood	0.19	0.006	0.006	0.003
35512	England	2013/14	B	B	575	ST-213 complex	CSF	0.19	0.016	0.008	0.006
35513	England	2013/14	Y	Y	23	ST-23 complex	Blood	0.094	0.004	0.008	0.008
35514	England	2013/14	B	B	213	ST-213 complex	Blood	0.19	0.006	0.008	0.008
35515	England	2013/14	B	B	269	ST-269 complex	Blood	0.125	0.016	0.008	0.008
35516	England	2013/14	B	B	213	ST-213 complex	Blood	0.064	0.016	0.008	0.004
35517	England	2013/14	Y	Y	114	ST-22 complex	Blood	0.094	0.012	0.008	0.008
35518	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.008	0.006
35519	England	2013/14	B	B	11250	ST-32 complex	Blood	0.064	0.016	0.006	0.004
35520	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.004
35521	England	2013/14	B	B	213	ST-213 complex	CSF	0.047	0.006	0.004	0.004
35522	England	2013/14	B	B	213	ST-213 complex	Blood	0.032	0.012	0.004	0.008
35523	England	2013/14	Y	Y	11254	ST-167 complex	Blood	0.047	0.006	0.006	0.008
35524	England	2013/14	C	C	9923	ST-60 complex	Blood	0.125	0.006	0.004	0.006
35525	England	2013/14	B	B	1161	ST-269 complex	CSF	0.125	0.012	0.006	0.008
35526	England	2013/14	B	B	485	ST-41/44 complex	Blood	0.125	0.008	0.004	0.004
35527	England	2013/14	B	B	2101	ST-213 complex	Blood	0.032	0.004	0.004	0.004
35528	England	2013/14	B	B	8023	ST-103 complex	Blood	0.094	0.008	0.006	0.004
35529	England	2013/14	B	B	11330	UA	CSF	0.047	0.008	0.004	0.004
35530	England	2013/14	B	B	11259	UA	Blood	0.064	0.012	0.004	0.004
35531	England	2013/14	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.006	0.008	0.008
35532	England	2013/14	B	B	485	ST-41/44 complex	Blood	0.19	0.008	0.006	0.004
35533	England	2013/14	B	B	2799	ST-41/44 complex	Blood	0.047	0.006	0.004	0.003
35534	England	2013/14	B	B	11261	ST-269 complex	CSF	0.19	0.008	0.006	0.006
35535	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.006
35536	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.006
35537	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.004
35538	England	2013/14	Y	Y	23	ST-23 complex	Blood	0.047	0.004	0.004	0.004
35539	England	2013/14	B	B	1194	ST-41/44 complex	Blood	0.047	0.004	0.006	0.003
35540	England	2013/14	B	B	11262	ST-213 complex	Blood	0.064	0.016	0.006	0.006
35541	England	2013/14	B	B	11263	ST-41/44 complex	CSF	0.016	0.008	0.004	<0.002
35542	England	2013/14	B	B	11265	ST-41/44 complex	Blood	0.023	0.003	0.004	0.003
35543	England	2013/14	Y	Y	23	ST-23 complex	Blood	0.064	0.006	0.006	0.004
35544	England	2013/14	B	B	1161	ST-269 complex	Blood	0.19	0.008	0.006	0.006
35545	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.006	0.006
35546	England	2013/14	B	B	32	ST-32 complex	Blood	0.064	0.016	0.006	0.006
35547	England	2013/14	Y	Y	1624	ST-167 complex	CSF	0.125	0.006	0.004	0.016
35548	England	2013/14	B	B	340	ST-41/44 complex	Blood	0.047	0.008	0.006	0.003
35549	England	2013/14	B	B	3446	ST-41/44 complex	Blood	0.064	0.008	0.006	0.006
35550	England	2013/14	B	B	6782	ST-41/44 complex	Blood	0.094	0.012	0.006	0.004
35551	England	2013/14	C	C	5133	ST-103 complex	Blood	0.023	0.064	0.006	0.002
35552	Wales	2013/14	B	B	5981	ST-41/44 complex	Blood	0.064	0.008	0.006	0.004
35553	England	2013/14	Y	Y	NK	INCOMPLETE MLST	Blood	0.094	0.008	0.004	0.006
35554	England	2013/14	B	B	34	ST-32 complex	Blood	0.047	0.008	0.006	0.006
35555	England	2013/14	B	B	1161	ST-269 complex	Blood	0.094	0.016	0.016	0.008
35556	England	2013/14	B	B	1403	ST-41/44 complex	Blood	0.064	0.023	0.006	0.008

35557	England	2013/14	B	B	2506	ST-32 complex	Blood	0.125	0.012	0.006	0.006
35558	England	2013/14	B	B	575	ST-213 complex	Blood	0.19	0.016	0.006	0.006
35559	England	2013/14	B	B	9242	ST-269 complex	CSF	0.064	0.004	0.006	0.006
35560	England	2013/14	W	W	2638	ST-22 complex	Blood	0.094	0.012	0.008	0.004
35561	England	2013/14	B	B	NK	INCOMPLETE MLST	Blood	0.064	0.012	0.008	0.003
35562	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.094	0.047	0.008	0.004
35563	Wales	2013/14	B	B	41	ST-41/44 complex	Blood	0.25	0.012	0.006	0.008
35564	England	2013/14	B	B	34	ST-32 complex	Blood	0.25	0.032	0.006	0.016
35565	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
35566	England	2013/14	B	B	154	ST-41/44 complex	Blood	0.064	0.012	0.006	0.006
35567	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.094	0.012	0.006	0.008
35568	England	2013/14	B	B	9180	ST-269 complex	Blood	0.25	0.008	0.012	0.012
35569	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.008	0.008
35570	Wales	2013/14	B	B	283	ST-269 complex	Blood	0.064	0.004	0.006	0.004
35571	England	2013/14	B	B	34	ST-32 complex	Blood	0.032	0.002	0.006	0.003
35572	England	2013/14	B	B	275	ST-269 complex	Blood	0.094	0.004	0.006	0.008
35573	England	2013/14	B	B	11266	ST-41/44 complex	CSF	0.19	0.012	0.008	0.008
35574	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.006	0.008
35575	England	2013/14	B	B	34	ST-32 complex	CSF	0.094	0.008	0.008	0.006
35576	England	2013/14	B	B	213	ST-213 complex	Blood	0.125	0.016	0.006	0.006
35577	Northern Ireland	2013/14	B	B	11865	ST-461 complex	Blood	0.38	0.094	0.006	0.012
35578	Wales	2013/14	B	B	5098	ST-41/44 complex	Blood	0.064	0.004	0.008	0.004
35579	England	2013/14	B	B	3116	ST-213 complex	Blood	0.094	0.012	0.006	0.004
35580	England	2013/14	B	B	461	ST-461 complex	Blood	0.25	0.003	0.006	0.006
35582	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.008	0.004
35583	England	2013/14	B	B	11272	ST-18 complex	Blood	0.125	0.032	0.008	0.016
35584	Northern Ireland	2013/14	B	B	5986	ST-41/44 complex	Blood	0.064	0.016	0.008	0.004
35585	England	2013/14	B	B	3447	ST-41/44 complex	Blood	0.064	0.008	0.008	0.008
35586	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.064	0.008	0.008	0.008
35587	England	2013/14	B	B	6789	ST-269 complex	Blood	0.064	0.002	0.008	0.004
35588	England	2013/14	B	B	749	ST-32 complex	Blood	0.25	0.008	0.008	0.008
35589	England	2013/14	B	B	32	ST-32 complex	Blood	0.064	0.032	0.008	0.006
35590	England	2013/14	Y	NK	23	ST-23 complex	Blood	0.032	0.064	0.008	0.008
35591	England	2013/14	Y	NK	23	ST-23 complex	Blood	0.094	0.004	0.006	0.006
35592	Wales	2013/14	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.008	0.006
35593	England	2013/14	C	C	467	ST-269 complex	CSF	0.064	0.016	0.008	0.006
35594	England	2013/14	B	B	1475	ST-41/44 complex	Blood	0.094	0.016	0.006	0.006
35595	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.006	0.004
35596	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.047	0.008	0.006	0.006
35597	England	2013/14	B	B	11460	ST-41/44 complex	CSF	0.064	0.006	0.006	0.004
35599	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.094	0.006	0.006	0.008
35600	England	2013/14	Y	Y	23	ST-23 complex	Blood	0.032	0.003	0.006	0.004
35601	England	2013/14	B	B	282	ST-282 complex	Blood	0.094	0.047	0.008	0.004
35602	England	2013/14	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.064	0.006	0.006
35603	England	2013/14	B	B	213	ST-213 complex	Blood	0.094	0.016	0.008	0.006
35604	England	2013/14	B	B	33	ST-32 complex	Blood	0.047	0.012	0.008	0.006
35605	England	2013/14	B	B	2455	ST-60 complex	Blood	0.023	0.016	0.008	0.006
35606	England	2013/14	B	B	5480	ST-41/44 complex	Blood	0.064	0.008	0.006	0.004
35607	England	2013/14	W	NK	114	ST-22 complex	Blood	0.125	0.008	0.008	0.006
35609	Northern Ireland	2013/14	B	B	9819	ST-41/44 complex	Blood	0.047	0.032	0.008	0.006
35610	England	2013/14	W	W	1617	ST-22 complex	Blood	0.064	0.012	0.008	0.006
35611	England	2013/14	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.008	0.006	0.008
35612	Wales	2013/14	B	B	1946	ST-461 complex	Blood	0.25	0.012	0.006	0.012
35613	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.19	0.003	0.006	0.016
35615	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.032	0.006	0.006	0.003
35616	England	2013/14	Y	Y	23	ST-23 complex	Blood	0.094	0.004	0.006	0.006
35617	England	2013/14	B	B	NK	INCOMPLETE MLST	Blood	0.047	0.008	0.008	0.004
35619	England	2013/14	B	B	11278	ST-32 complex	Blood	0.094	0.032	0.012	0.006
35620	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.094	0.006	0.008	0.008
35623	Northern Ireland	2013/14	B	B	1161	ST-269 complex	Blood	0.125	0.125	0.008	0.012
35625	England	2013/14	B	B	2314	ST-41/44 complex	Blood	0.125	0.004	0.008	0.006
35626	England	2013/14	B	B	8988	UA	Blood	0.19	0.047	0.012	0.006
35627	England	2013/14	Y	NK	1655	ST-23 complex	Blood	0.047	0.006	0.006	0.006
35628	Northern Ireland	2013/14	C	C	11	ST-11 complex	Blood	0.064	0.016	0.008	0.008
35629	Wales	2013/14	B	B	11279	ST-41/44 complex	Blood	0.064	0.008	0.006	0.006
35630	England	2013/14	B	B	269	ST-269 complex	Blood	0.047	0.032	0.006	0.003
35631	England	2013/14	B	B	1161	ST-269 complex	Blood	0.047	0.023	0.006	0.008
35633	England	2013/14	B	B	467	ST-269 complex	Blood	0.064	0.008	0.006	0.006
35636	England	2013/14	B	B	1774	ST-269 complex	Blood	0.064	0.008	0.008	0.008
35637	England	2013/14	Y	Y	11280	ST-23 complex	Blood	0.064	0.004	0.006	0.006
35639	Northern Ireland	2013/14	B	B	4145	ST-213 complex	Blood	0.064	0.016	0.006	0.006
35640	England	2013/14	B	B	1161	ST-269 complex	Blood	0.094	0.012	0.006	0.012
35641	Wales	2013/14	NG	E	11282	ST-1157 complex	Blood	0.064	0.032	0.004	0.006
35642	England	2013/14	Y	Y	23	ST-23 complex	CSF	0.094	0.006	0.004	0.012
35644	England	2013/14	B	B	NK	INCOMPLETE MLST	Blood	0.032	0.006	0.003	0.006
35645	England	2013/14	B	B	213	ST-213 complex	Blood	0.047	0.023	0.006	0.006
35646	England	2013/14	B	B	1423	ST-41/44 complex	Blood	0.094	0.012	0.006	0.008
35647	England	2013/14	B	B	7460	ST-32 complex	CSF	0.064	0.032	0.004	0.008
35648	Wales	2013/14	Y	Y	NK	INCOMPLETE MLST	Blood	0.094	0.008	0.006	0.012
35649	England	2013/14	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.004	0.004	0.006
35650	England	2013/14	C	C	11	ST-11 complex	Blood	0.25	0.023	0.006	0.012
35652	England	2013/14	C	C	NK	INCOMPLETE MLST	Blood	0.125	0.008	0.006	0.006
35653	England	2013/14	Y	NK	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.008
35654	England	2013/14	Y	Y	NK	INCOMPLETE MLST	Blood	0.047	0.004	0.006	0.008
35655	Wales	2013/14	B	B	8049	ST-32 complex	Blood	0.125	0.008	0.006	0.006

35656	England	2013/14	B	B	409	ST-41/44 complex	Blood	0.125	0.094	0.006	0.008
35657	England	2013/14	B	B	409	ST-41/44 complex	Blood	0.25	0.032	0.006	0.008
35658	England	2013/14	B	B	11291	ST-269 complex	Blood	0.047	0.006	0.006	0.004
35659	England	2013/14	C	C	10482	ST-11 complex	Joint	0.064	0.032	0.006	0.008
35660	Wales	2013/14	Y	Y	1655	ST-23 complex	Blood	0.064	0.016	0.006	0.006
35661	England	2013/14	W	W	22	ST-22 complex	Blood	0.064	0.006	0.004	0.003
35662	England	2013/14	B	B	275	ST-269 complex	Blood	0.125	0.004	0.006	0.006
35663	England	2013/14	B	B	162	ST-162 complex	Blood	0.047	0.016	0.006	0.004
35665	England	2013/14	Y	Y	11293	ST-23 complex	Blood	0.032	0.004	0.004	0.006
35666	England	2013/14	B	B	32	ST-32 complex	CSF	0.064	0.008	0.006	0.008
35667	Wales	2013/14	B	B	11	ST-11 complex	Blood	0.094	0.094	0.006	0.012
35668	England	2013/14	B	B	162	ST-162 complex	Blood	0.064	0.016	0.006	0.004
35669	England	2013/14	B	B	1161	ST-269 complex	Blood	0.032	0.023	0.006	0.004
35671	England	2013/14	B	B	NK	INCOMPLETE MLST	Blood	0.047	0.006	0.006	0.004
35672	England	2013/14	C	C	11	ST-11 complex	Blood	0.064	0.016	0.006	0.008
35673	England	2013/14	B	B	1194	ST-41/44 complex	Blood	0.032	0.032	0.004	0.003
35677	England	2013/14	B	B	1161	ST-269 complex	Blood	0.25	0.064	0.006	0.008
35678	England	2013/14	B	B	NK	INCOMPLETE MLST	Joint	0.064	0.032	0.004	0.006
35679	England	2013/14	B	B	1089	ST-269 complex	Blood	0.032	0.064	0.006	0.004
35680	England	2013/14	B	B	275	ST-269 complex	Blood	0.094	0.008	0.004	0.006
35681	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.047	0.008	0.004	0.004
35682	England	2013/14	B	B	34	ST-32 complex	Blood	0.064	0.032	0.008	0.006
35683	Wales	2013/14	B	B	1096	ST-32 complex	CSF	0.064	0.064	0.006	0.006
35684	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.064	0.008	0.004	0.006
35685	England	2013/14	Y	Y	767	ST-167 complex	Blood	0.047	0.006	0.004	0.006
35688	England	2013/14	C	C	11	ST-11 complex	Blood	0.094	0.008	0.006	0.012
35691	England	2013/14	Y	Y	NK	INCOMPLETE MLST	Blood	0.094	0.008	0.004	0.006
35692	England	2013/14	Y	Y	1655	ST-23 complex	Joint	0.064	0.004	0.004	0.004
35693	England	2013/14	C	C	11	ST-11 complex	Blood	0.047	0.016	0.006	0.006
35694	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.004
35695	England	2013/14	B	B	5391	UA	Blood	0.023	0.004	0.003	0.006
35696	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.003	0.008
35697	England	2013/14	Y	Y	114	ST-22 complex	Blood	0.064	0.012	0.006	0.008
35698	England	2013/14	B	B	11296	ST-60 complex	Blood	0.032	0.016	0.003	0.004
35699	England	2013/14	B	B	4786	ST-32 complex	CSF	0.19	0.012	0.006	0.008
35701	England	2013/14	B	B	275	ST-269 complex	CSF	0.064	0.012	0.006	0.008
35703	England	2013/14	B	B	213	ST-213 complex	Joint	0.19	0.006	0.004	0.008
35704	England	2013/14	B	B	8511	ST-41/44 complex	Blood	0.047	0.012	0.006	0.004
35705	England	2013/14	B	B	11297	ST-41/44 complex	Blood	0.023	0.047	0.004	0.003
35706	England	2013/14	C	C	11	ST-11 complex	Blood	0.125	0.032	0.004	0.016
35707	England	2013/14	C	C	11298	ST-334 complex	Blood	0.094	0.064	0.006	0.006
35708	England	2013/14	B	B	2922	ST-41/44 complex	Blood	0.25	0.016	0.006	0.012
35709	England	2013/14	W/Y	W/Y	1655	ST-23 complex	Blood	0.064	0.006	0.006	0.008
35710	England	2013/14	B	B	60	ST-60 complex	Blood	0.032	0.016	0.008	0.008
35711	England	2013/14	B	B	11429	UA	Blood	0.25	0.008	0.006	0.016
35712	England	2013/14	B	B	213	ST-213 complex	Blood	0.047	0.064	0.008	0.006
35713	England	2013/14	B	B	1946	ST-461 complex	Blood	0.75	0.094	0.006	0.016
35714	England	2013/14	B	B	11299	UA	Blood	0.064	0.012	0.006	0.006
35715	England	2013/14	B	B	11300	ST-213 complex	Blood	0.047	0.032	0.006	0.004
35716	England	2013/14	B	B	1161	ST-269 complex	Blood	0.047	0.023	0.008	0.012
35717	England	2013/14	Y	Y	910	UA	Blood	0.125	0.016	0.004	0.012
35718	England	2013/14	B	B	213	ST-213 complex	Blood	0.25	0.012	0.004	0.006
35719	England	2013/14	B	B	5981	ST-41/44 complex	Blood	0.064	0.008	0.006	0.004
35720	England	2013/14	B	B	11301	UA	Joint	0.064	0.023	0.003	0.004
35721	England	2013/14	Y	Y	11331	ST-23 complex	Blood	0.047	0.006	0.004	0.003
35723	England	2013/14	B	B	1159	UA	Blood	0.094	0.032	0.006	0.008
35724	England	2013/14	B	B	11302	ST-32 complex	Blood	0.19	0.016	0.006	0.016
35726	England	2013/14	B	B	275	ST-269 complex	Blood	0.094	0.012	0.006	0.004
35727	Wales	2013/14	B	B	1946	ST-461 complex	Blood	0.38	0.023	0.004	0.012
35729	Northern Ireland	2013/14	B	B	NK	INCOMPLETE MLST	Blood	0.064	0.006	0.006	0.006
35730	England	2013/14	B	B	5151	UA	Blood	0.25	0.006	0.006	0.008
35731	Wales	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
35732	England	2013/14	B	B	1194	ST-41/44 complex	Blood	0.047	0.023	0.006	0.004
35733	England	2013/14	B	B	213	ST-213 complex	Blood	0.19	0.023	0.004	0.006
35734	Wales	2013/14	B	B	461	ST-461 complex	CSF	0.094	0.064	0.004	0.012
35735	Wales	2013/14	B	B	41	ST-41/44 complex	Blood	0.047	0.023	0.008	0.004
35736	Wales	2013/14	B	B	11303	UA	Blood	0.19	0.012	0.004	0.004
35737	England	2013/14	B	B	11304	ST-269 complex	Blood	0.19	0.012	0.004	0.012
35738	England	2013/14	W	W	NK	INCOMPLETE MLST	Blood	0.125	0.003	0.004	0.002
35739	England	2013/14	B	B	461	ST-461 complex	Blood	0.19	0.016	0.004	0.008
35740	England	2013/14	B	B	269	ST-269 complex	Blood	0.047	0.008	0.008	0.004
35741	England	2013/14	B	B	NK	INCOMPLETE MLST	Blood	0.125	0.016	0.006	0.004
35742	England	2013/14	B	B	4051	UA	Blood	0.125	0.023	0.004	0.006
35743	England	2014/15	B	B	213	ST-213 complex	Blood	0.047	0.016	0.004	0.003
35744	England	2014/15	B	B	NK	INCOMPLETE MLST	Blood	0.094	0.016	0.004	0.004
35746	Wales	2014/15	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.006	0.006
35747	England	2014/15	B	B	213	ST-213 complex	Blood	0.047	0.023	0.004	0.004
35748	England	2014/15	B	B	8061	UA	Blood	0.25	0.006	0.003	0.016
35749	England	2014/15	B	B	33	ST-32 complex	Blood	0.094	0.012	0.006	0.006
35750	England	2014/15	B	B	1946	ST-461 complex	Blood	0.38	0.012	0.004	0.006
35751	England	2014/15	B	B	NK	INCOMPLETE MLST	Blood	0.25	0.012	0.006	0.012
35752	England	2014/15	B	B	340	ST-41/44 complex	Blood	0.047	0.016	0.003	0.003
35753	England	2014/15	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.008	0.006	0.004
35755	England	2014/15	B	B	1161	ST-269 complex	Blood	0.064	0.008	0.006	0.006
35757	Wales	2014/15	B	B	213	ST-213 complex	Blood	0.023	0.004	0.003	0.003

35758	Wales	2014/15	B	B	43	ST-41/44 complex	Blood	0.047	0.002	0.004	0.047
35759	England	2014/15	B	B	1194	ST-41/44 complex	CSF	0.032	0.004	0.004	0.003
35760	England	2014/15	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.004	0.004	0.004
35761	England	2014/15	Y	Y	23	ST-23 complex	Blood	0.19	0.004	0.004	0.006
35762	Northern Ireland	2014/15	C	C	11	ST-11 complex	Joint	0.047	0.004	0.008	0.004
35764	England	2014/15	B	B	NK	INCOMPLETE MLST	Blood	0.047	0.004	0.006	0.003
35765	England	2014/15	B	B	269	ST-269 complex	Blood	0.047	0.008	0.006	0.003
35766	England	2014/15	B	B	485	ST-41/44 complex	Blood	0.125	0.008	0.006	0.006
35767	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.006
35768	Wales	2014/15	B	B	5986	ST-41/44 complex	Blood	0.094	0.016	0.004	0.006
35769	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.047	0.004	0.004	0.004
35770	England	2014/15	B	B	1161	ST-269 complex	Blood	0.047	0.012	0.003	0.004
35771	England	2014/15	B	B	485	ST-41/44 complex	Blood	0.19	0.003	0.006	0.006
35772	England	2014/15	Y	Y	NK	INCOMPLETE MLST	Blood	0.032	0.004	0.004	0.003
35773	England	2014/15	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.004	0.004	0.004
35774	England	2014/15	B	B	269	ST-269 complex	Blood	0.023	0.008	0.006	0.002
35775	England	2014/15	C	C	11	ST-11 complex	Blood	0.064	0.023	0.094	0.006
35776	England	2014/15	B	B	1157	ST-1157 complex	Blood	0.032	0.008	0.004	0.004
35777	England	2014/15	C	C	11332	ST-116 complex	Blood	0.032	0.064	0.004	0.002
35778	England	2014/15	B	B	11305	ST-269 complex	Blood	0.023	0.008	0.006	0.002
35779	Northern Ireland	2014/15	B	B	1214	ST-269 complex	Blood	0.064	0.016	0.006	0.004
35780	England	2014/15	B	B	485	ST-41/44 complex	Blood	0.064	0.047	0.004	0.002
35781	England	2014/15	B	B	1946	ST-461 complex	Blood	0.19	0.012	0.004	0.004
35783	England	2014/15	B	B	11306	UA	Blood	0.094	0.016	0.008	0.006
35784	England	2014/15	B	B	11307	UA	Blood	0.094	0.004	0.004	0.006
35785	Wales	2014/15	B	B	8049	ST-32 complex	Blood	0.25	0.006	0.004	0.004
35787	England	2014/15	B	B	11308	ST-269 complex	Blood	0.008	0.006	0.004	0.002
35789	England	2014/15	B	B	8054	ST-41/44 complex	Blood	0.016	0.002	0.19	0.003
35790	England	2014/15	B	B	8054	ST-41/44 complex	Blood	0.064	0.006	0.004	0.004
35791	England	2014/15	W	W	22	ST-22 complex	Blood	0.064	0.047	0.004	0.004
35793	England	2014/15	B	B	11309	ST-41/44 complex	Blood	0.047	0.012	0.003	0.004
35794	England	2014/15	B	B	340	ST-41/44 complex	Blood	0.016	0.008	0.004	0.003
35795	England	2014/15	B	B	485	ST-41/44 complex	Blood	0.125	0.008	0.004	0.004
35797	England	2014/15	B	B	11302	ST-32 complex	Blood	0.125	0.006	0.004	0.008
35798	England	2014/15	B	B	162	ST-162 complex	Blood	0.047	0.012	0.008	0.004
35802	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
35803	England	2014/15	B	B	1423	ST-41/44 complex	Blood	0.064	0.006	0.006	0.006
35804	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.006	0.006
35805	England	2014/15	B	B	340	ST-41/44 complex	Blood	0.047	0.012	0.006	0.006
35830	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.006	0.004
37662	England	2013/14	B	B	213	ST-213 complex	Blood	0.047	0.012	0.006	0.004
37663	Wales	2013/14	B	B	41	ST-41/44 complex	Blood	0.094	0.064	0.004	0.012
37664	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.047	0.008	0.004	0.006
37665	England	2013/14	B	B	1161	ST-269 complex	Blood	0.064	0.004	0.006	0.008
37666	England	2013/14	Y	Y	23	ST-23 complex	Blood	0.064	0.006	0.004	0.008
37667	England	2013/14	Y	Y	1655	ST-23 complex	Blood	0.094	0.004	0.006	0.012
37668	England	2013/14	C	C	11	ST-11 complex	Blood	0.064	0.006	0.008	0.008
37669	England	2013/14	B	B	41	ST-41/44 complex	Blood	0.19	0.032	0.006	0.008
37672	England	2014/15	Y	NG	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
37674	England	2014/15	B	B	275	ST-269 complex	Blood	0.19	0.006	0.004	0.006
37676	England	2014/15	Y	NK	1624	ST-167 complex	Blood	0.064	0.004	0.006	0.008
37677	England	2014/15	B	B	275	ST-269 complex	Blood	0.064	0.006	0.004	0.004
37678	England	2014/15	B	B	1097	ST-41/44 complex	Blood	0.047	0.008	0.006	0.004
37679	England	2014/15	C	C	11	ST-11 complex	Blood	0.19	0.023	0.006	0.008
37680	England	2014/15	B	B	11465	ST-213 complex	Blood	0.125	0.008	0.006	0.008
37682	England	2014/15	B	B	2506	ST-32 complex	Blood	0.125	0.006	0.006	0.008
37683	England	2014/15	B	B	10817	ST-162 complex	Blood	0.25	0.008	0.006	0.006
37684	England	2014/15	B	B	1194	ST-41/44 complex	Blood	0.032	0.006	0.006	0.003
37686	England	2014/15	B	B	3754	ST-41/44 complex	Blood	0.047	0.006	0.004	0.003
37687	Wales	2014/15	C	C	32	ST-32 complex	Blood	0.047	0.064	0.006	0.004
37688	England	2014/15	B	B	1163	ST-269 complex	Blood	0.047	0.008	0.006	0.004
37689	England	2014/15	Y	Y	11866	ST-23 complex	Blood	0.047	0.004	0.004	0.004
37691	England	2014/15	Y	NK	23	ST-23 complex	Spleen	0.047	0.002	0.004	0.004
37694	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.047	0.012	0.006	0.004
37696	England	2014/15	B	B	32	ST-32 complex	Blood	0.047	0.012	0.006	0.004
37697	England	2014/15	Y	Y	3582	ST-23 complex	Blood	0.064	0.004	0.004	0.004
37698	England	2014/15	B	B	269	ST-269 complex	Blood	0.023	0.004	0.004	0.002
37700	England	2014/15	B	B	3754	ST-41/44 complex	Blood	0.032	0.006	0.004	0.002
37702	England	2014/15	B	B	136	ST-41/44 complex	Blood	0.047	0.006	0.004	0.002
37703	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.003	0.002
37704	England	2014/15	B	B	1161	ST-269 complex	CSF	0.19	0.008	0.004	0.004
37705	England	2014/15	B	B	1111	UA	Joint	0.38	0.032	0.006	0.032
37706	England	2014/15	B	B	11466	ST-269 complex	Blood	0.032	0.006	0.006	0.004
37707	England	2014/15	B	B	154	ST-41/44 complex	Blood	0.032	0.006	0.004	0.004
37709	England	2014/15	C	C	11	ST-11 complex	Blood	0.064	0.006	0.006	0.004
37712	England	2014/15	B	B	11467	ST-41/44 complex	Blood	0.047	0.006	0.006	0.004
37713	England	2014/15	Y	NK	NK	INCOMPLETE MLST	Blood	0.19	0.004	0.003	0.008
37714	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.064	0.006	0.006	0.008
37715	England	2014/15	B	B	1754	ST-60 complex	Blood	0.032	0.006	0.003	0.004
37718	England	2014/15	B	B	46	ST-41/44 complex	Blood	0.064	0.008	0.008	0.004
37719	England	2014/15	B	B	1097	ST-41/44 complex	Blood	0.047	0.008	0.006	0.004
37720	England	2014/15	B	B	5151	UA	Blood	0.125	0.008	0.008	0.008
37721	Wales	2014/15	B	B	11468	ST-461 complex	Blood	0.25	0.016	0.006	0.008
37723	England	2014/15	B	B	60	ST-60 complex	Blood	0.032	0.003	0.008	0.004
37724	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.064	0.012	0.008	0.004

37725	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.023	0.003	0.008	0.002
37726	England	2014/15	B	B	3635	ST-213 complex	Blood	0.094	0.006	0.004	0.004
37727	England	2014/15	B	B	6058	ST-41/44 complex	Blood	0.25	0.012	0.006	0.008
37728	England	2014/15	C	C	11	ST-11 complex	Blood	0.064	0.004	0.006	0.002
37729	England	2014/15	Y	Y	1466	ST-174 complex	Blood	0.047	0.006	0.002	0.004
37730	Northern Ireland	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
37733	England	2014/15	B	B	9881	ST-213 complex	Blood	0.064	0.008	0.006	0.004
37734	England	2014/15	B	B	32	ST-32 complex	Blood	0.064	0.006	0.006	0.004
37735	England	2014/15	B	B	3200	ST-4821 complex	Blood	0.38	0.023	0.008	0.008
37737	England	2014/15	B	B	409	ST-41/44 complex	Blood	0.19	0.064	0.008	0.008
37740	England	2014/15	W	NK	184	ST-22 complex	CSF	0.125	0.016	0.008	0.004
37741	England	2014/15	B	B	5342	ST-32 complex	Blood	0.032	0.006	0.008	0.004
37743	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.125	0.003	0.006	0.004
37744	England	2014/15	B	B	11469	UA	Blood	0.047	0.003	0.003	0.004
37745	England	2014/15	B	B	749	ST-32 complex	Blood	0.094	0.006	0.004	0.004
37750	England	2014/15	B	NG	290	ST-32 complex	Blood	0.094	0.012	0.008	0.006
37751	England	2014/15	Y	NK	23	ST-23 complex	Blood	0.064	0.008	0.006	0.006
37752	England	2014/15	C	C	11	ST-11 complex	Blood	0.19	0.023	0.008	0.006
37753	England	2014/15	B	B	1214	ST-269 complex	Blood	0.032	0.032	0.008	0.002
37755	England	2014/15	B	B	1163	ST-269 complex	Blood	0.047	0.004	0.006	0.004
37756	England	2014/15	B	B	32	ST-32 complex	Blood	0.19	0.006	0.006	0.004
37758	England	2014/15	C	C	11	ST-11 complex	Blood	0.19	0.032	0.008	0.008
37761	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.125	0.004	0.006	<0.002
37762	England	2014/15	B	NG	11470	ST-269 complex	Blood	0.19	0.003	0.004	0.002
37763	England	2014/15	C	C	11	ST-11 complex	Blood	0.094	0.012	0.004	0.006
37764	Northern Ireland	2014/15	W	NK	11	ST-11 complex	Blood	0.032	0.003	0.006	0.002
37765	England	2014/15	Y	NK	11868	ST-23 complex	Blood	0.125	0.004	0.004	0.012
37766	England	2014/15	B	B	11471	ST-269 complex	CSF	0.064	0.003	0.004	0.003
37767	England	2014/15	B	B	8380	ST-41/44 complex	Blood	0.064	0.004	0.008	0.004
37768	England	2014/15	Y	NK	11472	ST-23 complex	Blood	0.064	0.008	0.008	0.006
37771	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.032	0.003	0.004	0.004
37772	England	2014/15	B	B	485	ST-41/44 complex	Blood	0.094	0.006	0.006	0.003
37773	England	2014/15	B	B	18	ST-18 complex	CSF	0.032	0.002	0.006	0.002
37775	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.19	0.004	0.004	0.006
37776	England	2014/15	B	B	11473	ST-269 complex	Blood	0.125	0.004	0.006	0.006
37777	England	2014/15	B	B	1157	ST-1157 complex	Blood	0.064	0.012	0.004	0.003
37779	England	2014/15	B	B	11869	ST-41/44 complex	CSF	0.125	0.004	0.004	0.004
37780	England	2014/15	B	B	1946	ST-461 complex	Blood	0.25	0.006	0.002	0.016
37781	England	2014/15	B	B	1161	ST-269 complex	CSF	0.19	0.003	0.006	0.006
37782	England	2014/15	B	B	275	ST-269 complex	CSF	0.032	0.008	0.006	0.002
37783	England	2014/15	B	B	278	ST-35 complex	Blood	0.094	0.004	0.004	0.003
37785	England	2014/15	B	B	3989	UA	Blood	0.19	0.012	0.004	0.006
37786	England	2014/15	Y	NK	1624	ST-167 complex	Blood	0.125	0.003	0.006	0.012
37787	England	2014/15	C	C	11	ST-11 complex	Blood	0.032	0.008	0.006	0.006
37788	England	2014/15	B	B	213	ST-213 complex	Blood	0.047	0.008	0.006	0.003
37789	England	2014/15	B	B	34	ST-32 complex	Blood	0.125	0.006	0.006	0.012
37790	England	2014/15	B	B	1161	ST-269 complex	Blood	0.064	0.032	0.008	0.004
37791	England	2014/15	B	B	1354	ST-269 complex	Blood	0.032	0.004	0.006	0.002
37792	England	2014/15	B	B	1157	ST-1157 complex	Blood	0.047	0.008	0.006	0.004
37794	England	2014/15	Y	NG	1655	ST-23 complex	Blood	0.064	0.004	0.006	0.004
37795	Wales	2014/15	Y	Y	23	ST-23 complex	CSF	0.25	0.004	0.006	0.016
37796	England	2014/15	Y	NK	23	ST-23 complex	Blood	0.094	0.006	0.006	0.004
37800	England	2014/15	B	B	1161	ST-269 complex	Blood	0.19	0.008	0.008	0.006
37802	England	2014/15	B	B	485	ST-41/44 complex	Blood	0.125	0.004	0.006	0.004
37803	England	2014/15	B	B	485	ST-41/44 complex	CSF	0.064	0.012	0.006	0.003
37804	England	2014/15	B	B	NK	INCOMPLETE MLST	Blood	0.047	0.008	0.006	0.003
37807	England	2014/15	B	B	162	ST-162 complex	Blood	0.064	0.006	0.008	0.003
37808	England	2014/15	Y	NK	11474	ST-167 complex	Blood	0.047	0.002	0.004	0.003
37810	England	2014/15	Y	Y	168	ST-167 complex	Blood	0.064	0.004	0.004	0.004
37812	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.047	0.004	0.006	0.003
37813	England	2014/15	Y	Y	1624	ST-167 complex	Blood	0.032	0.003	0.006	0.003
37814	England	2014/15	B	B	485	ST-41/44 complex	Blood	0.19	0.008	0.002	0.002
37815	England	2014/15	C	C	11	ST-11 complex	Blood	0.064	0.004	0.002	0.002
37816	England	2014/15	C	C	11	ST-11 complex	Blood	0.19	0.006	0.002	0.002
37817	England	2014/15	B	B	11475	UA	Blood	0.023	0.004	0.002	0.002
37818	England	2014/15	B	B	213	ST-213 complex	Blood	0.064	0.012	0.002	0.002
37819	England	2014/15	B	B	1774	ST-269 complex	Blood	0.047	0.004	0.002	0.002
37820	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.094	0.006	0.002	0.002
37823	England	2014/15	B	B	11302	ST-32 complex	Blood	0.125	0.002	0.002	0.016
37824	England	2014/15	B	B	9176	ST-213 complex	Blood	0.064	0.004	0.002	0.016
37825	England	2014/15	Y	Y	NK	INCOMPLETE MLST	Blood	0.047	0.002	0.002	0.016
37827	England	2014/15	Y	NK	23	ST-23 complex	Blood	0.25	0.002	0.002	0.002
37829	Northern Ireland	2014/15	B	B	11870	ST-269 complex	Blood	0.064	0.006	0.002	0.016
37830	England	2014/15	B	B	1163	ST-269 complex	Blood	0.125	0.006	0.002	0.016
37831	England	2014/15	B	B	162	ST-162 complex	Blood	0.064	0.012	0.002	0.016
37832	England	2014/15	B	B	103	ST-103 complex	Joint	0.023	0.004	0.002	0.002
37833	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.064	0.006	0.002	0.006
37835	England	2014/15	B	B	1163	ST-269 complex	Blood	0.064	0.004	0.002	0.006
37836	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.002	0.006
37837	Wales	2014/15	B	B	1161	ST-269 complex	Blood	0.094	0.006	0.002	0.006
37838	England	2014/15	Y	NK	1655	ST-23 complex	Joint	0.064	0.004	0.002	0.008
37839	England	2014/15	B	B	11476	UA	Blood	0.032	0.002	0.002	0.004
37840	England	2014/15	W	W	3849	ST-22 complex	Blood	0.125	0.016	0.002	0.004
37841	England	2014/15	Y	NK	23	ST-23 complex	Blood	0.064	0.004	0.002	0.004
37842	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.064	0.006	0.002	0.003

37843	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.002	0.006
37844	England	2014/15	B	B	1096	ST-32 complex	Blood	0.064	0.006	0.002	0.006
37845	Wales	2014/15	W	NK	11	ST-11 complex	Blood	0.125	0.016	0.002	0.012
37846	England	2014/15	B	B	213	ST-213 complex	Blood	0.064	0.012	0.002	0.004
37847	England	2014/15	Y	Y	23	ST-23 complex	Joint	0.047	0.023	0.002	0.006
37848	England	2014/15	B	NG	1096	ST-32 complex	Blood	0.064	0.004	0.002	0.006
37849	England	2014/15	B	B	11477	ST-41/44 complex	Blood	0.094	0.004	0.002	0.006
37850	England	2014/15	Y	NK	23	ST-23 complex	CSF	0.125	0.003	0.002	0.006
37851	England	2014/15	Y	NK	1624	ST-167 complex	Blood	0.125	0.006	0.002	0.023
37852	Wales	2014/15	B	B	1194	ST-41/44 complex	CSF	0.047	0.008	0.002	0.004
37853	England	2014/15	Y	NK	23	ST-23 complex	Blood	0.064	0.006	0.002	0.004
37858	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.064	0.006	0.002	0.006
37859	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.094	0.006	0.002	0.008
37863	England	2014/15	Y	NK	1466	ST-174 complex	Blood	0.064	0.016	0.002	0.008
37864	Wales	2014/15	W	W	184	ST-22 complex	Blood	0.094	0.023	0.002	0.006
37865	England	2014/15	B	NG	41	ST-41/44 complex	Blood	0.094	0.004	0.002	0.008
37866	Wales	2014/15	W	NK	11	ST-11 complex	Blood	0.064	0.008	0.008	0.006
37867	England	2014/15	Y	NK	23	ST-23 complex	Joint	0.064	0.004	0.002	0.004
37869	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.032	0.002	0.002	0.002
37871	Northern Ireland	2014/15	B	B	269	ST-269 complex	Blood	0.047	0.003	0.002	0.003
37872	England	2014/15	B	B	1946	ST-461 complex	Blood	0.094	0.002	0.002	0.004
37874	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.094	0.003	0.002	0.002
37876	England	2014/15	B	B	269	ST-269 complex	Blood	0.047	0.012	0.012	0.004
37877	England	2014/15	B	B	11478	ST-162 complex	Blood	0.064	0.008	0.008	0.004
37878	England	2014/15	B	B	11479	ST-213 complex	Blood	0.023	0.004	0.003	0.003
37880	England	2014/15	B	B	8956	ST-32 complex	Blood	0.064	0.006	0.006	0.004
37883	Wales	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.006	0.006	0.006
37884	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.094	0.003	0.003	0.003
37885	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.008
37886	England	2014/15	B	B	2100	ST-213 complex	Blood	0.032	0.004	0.004	0.004
37887	England	2014/15	B	B	1052	UA	Blood	0.032	0.004	0.006	0.002
37888	England	2014/15	B	B	269	ST-269 complex	Blood	0.047	0.016	0.004	0.004
37889	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.008
37892	England	2014/15	NG	NG	23	ST-23 complex	Blood	0.094	0.004	0.004	0.004
37894	England	2014/15	C	C	11	ST-11 complex	Blood	0.125	0.006	0.004	0.006
37895	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.047	0.012	0.006	0.006
37896	England	2014/15	B	B	60	ST-60 complex	Blood	0.064	0.006	0.006	0.006
37897	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.032	0.003	0.004	0.004
37898	England	2014/15	B	B	6135	ST-41/44 complex	CSF	0.023	0.004	0.006	0.003
37899	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.006	0.006
37900	England	2014/15	B	B	863	UA	Blood	0.25	0.012	0.008	0.012
37901	England	2014/15	B	B	213	ST-213 complex	Blood	0.125	0.016	0.008	0.008
37903	England	2014/15	B	B	749	ST-32 complex	Blood	0.094	0.004	0.006	0.008
37905	England	2014/15	B	B	213	ST-213 complex	Blood	0.094	0.012	0.006	0.006
37906	England	2014/15	B	B	9352	ST-41/44 complex	Blood	0.094	0.008	0.006	0.006
37908	England	2014/15	B	B	NK	INCOMPLETE MLST	CSF	0.125	0.006	0.006	0.008
37909	England	2014/15	B	B	3282	ST-213 complex	Blood	0.047	0.003	0.004	0.006
37911	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
37912	England	2014/15	B	B	1764	ST-35 complex	Blood	0.047	0.006	0.004	0.002
37913	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.19	0.008	0.004	0.004
37914	England	2014/15	W	NK	1655	ST-23 complex	Blood	0.032	0.004	0.006	0.004
37916	England	2014/15	B	B	4971	ST-41/44 complex	Blood	0.047	0.006	0.006	0.002
37917	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.125	0.003	0.006	0.004
37918	Northern Ireland	2014/15	C	C	11	ST-11 complex	Blood	0.047	0.016	0.006	0.004
37919	England	2014/15	B	B	11480	UA	Blood	0.064	0.012	0.004	0.004
37920	England	2014/15	B	B	1214	ST-269 complex	Blood	0.023	0.004	0.004	0.002
37921	England	2014/15	B	B	340	ST-41/44 complex	Blood	0.032	0.008	0.006	0.004
37923	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.047	0.004	0.006	0.004
37924	England	2014/15	B	B	275	ST-269 complex	Blood	0.032	0.032	0.006	0.004
37925	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.094	0.012	0.006	0.004
37926	England	2014/15	Y	Y	10458	ST-23 complex	Blood	0.064	0.006	0.006	0.004
37927	England	2014/15	B	B	11481	ST-35 complex	CSF	0.047	0.008	0.006	0.004
37928	Northern Ireland	2014/15	B	B	2693	ST-269 complex	Blood	0.047	0.008	0.006	0.002
37929	England	2014/15	B	B	162	ST-162 complex	Blood	0.047	0.016	0.008	0.004
37931	England	2014/15	B	B	467	ST-269 complex	Blood	0.047	0.008	0.006	0.002
37934	Wales	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.008	0.006	0.004
37935	Wales	2014/15	B	B	213	ST-213 complex	Blood	0.032	0.006	0.004	0.002
37937	England	2014/15	Y	NK	11	ST-11 complex	Blood	0.047	0.008	0.008	0.002
37938	England	2014/15	Y	NK	23	ST-23 complex	Blood	0.047	0.004	0.006	0.004
37939	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.064	0.008	0.006	0.008
37941	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.064	0.006	0.006	0.004
37943	England	2014/15	B	B	269	ST-269 complex	Blood	0.047	0.008	0.008	0.002
37944	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.064	0.006	0.006	0.004
37945	England	2014/15	B	B	154	ST-41/44 complex	Blood	0.032	0.006	0.006	0.002
37946	England	2014/15	NG	Z	2123	UA	Blood	0.094	0.016	0.006	0.008
37947	England	2014/15	B	B	11482	ST-364 complex	Blood	0.032	0.003	0.006	0.002
37948	England	2014/15	C	C	11024	ST-269 complex	Blood	0.032	0.023	0.004	0.002
37949	England	2014/15	C	C	11	ST-11 complex	Blood	0.047	0.008	0.006	0.004
37950	England	2014/15	B	NG	213	ST-213 complex	Blood	0.047	0.032	0.004	0.002
37952	England	2014/15	B	B	1991	ST-269 complex	Blood	0.094	0.012	0.008	0.002
37953	England	2014/15	B	B	485	ST-41/44 complex	CSF	0.19	0.008	0.006	0.002
37954	Northern Ireland	2014/15	B	B	1163	ST-269 complex	Blood	0.047	0.023	0.006	0.002
37956	England	2014/15	B	B	213	ST-213 complex	Blood	0.047	0.012	0.004	0.004
37957	England	2014/15	B	B	213	ST-213 complex	Blood	0.047	0.012	0.006	0.004
37959	England	2014/15	B	B	1946	ST-461 complex	Blood	0.19	0.032	0.006	0.008

37960	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.047	0.008	0.006	0.004
37963	England	2014/15	Y	NK	23	ST-23 complex	Blood	0.094	0.008	0.006	0.004
37964	England	2014/15	W	W	9316	UA	Blood	0.047	0.006	0.004	0.004
37965	Northern Ireland	2014/15	B	B	274	ST-41/44 complex	Blood	0.032	0.016	0.006	0.004
37966	England	2014/15	B	B	35	ST-35 complex	Blood	0.19	0.003	0.004	0.012
37967	England	2014/15	C	C	11	ST-11 complex	Blood	0.047	0.012	0.006	0.004
37968	England	2014/15	B	B	5815	ST-35 complex	Blood	0.064	0.008	0.006	0.004
37969	England	2014/15	B	B	11871	ST-213 complex	Blood	0.064	0.023	0.006	0.004
37970	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.094	0.008	0.006	0.004
37971	England	2014/15	B	B	749	ST-32 complex	Blood	0.19	0.004	0.004	0.004
37972	Northern Ireland	2014/15	B	B	1161	ST-269 complex	Blood	0.25	0.012	0.008	0.004
37973	England	2014/15	B	B	NK	INCOMPLETE MLST	Blood	0.064	0.012	0.006	0.002
37974	England	2014/15	C	C	11024	ST-269 complex	Joint	0.032	0.016	0.006	0.002
37975	England	2014/15	B	B	1161	ST-269 complex	CSF	0.047	0.008	0.006	0.002
37976	England	2014/15	B	B	269	ST-269 complex	Blood	0.064	0.006	0.006	0.004
37979	England	2014/15	Y	Y	4183	ST-23 complex	Blood	0.047	0.004	0.004	0.004
37982	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.002
37984	England	2014/15	B	B	11872	ST-35 complex	Blood	0.25	0.003	0.004	0.004
37985	England	2014/15	B	B	1161	ST-269 complex	CSF	0.125	0.006	0.004	0.004
37986	Northern Ireland	2014/15	W	W	11	ST-11 complex	Joint	0.064	0.004	0.006	0.004
37989	England	2014/15	B	B	479	ST-269 complex	Blood	0.047	0.006	0.006	0.002
37991	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.047	0.008	0.004	0.002
37993	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.006	0.002
37994	England	2014/15	B	B	11483	UA	Blood	0.064	0.006	0.008	0.002
37996	England	2014/15	B	B	11889	UA	CSF	0.094	0.012	0.006	0.003
37997	England	2014/15	B	B	213	ST-213 complex	Blood	0.25	0.016	0.008	0.004
38000	England	2014/15	B	B	749	ST-32 complex	Blood	0.19	0.012	0.006	0.004
38002	England	2014/15	B	B	7622	UA	Blood	0.047	0.016	0.006	0.002
38005	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.064	0.008	0.006	0.004
38006	England	2014/15	B	B	1161	ST-269 complex	Blood	0.125	0.008	0.008	0.006
38009	England	2014/15	B	B	340	ST-41/44 complex	Blood	0.047	0.012	0.008	0.004
38010	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.094	0.006	0.006	0.004
38012	England	2014/15	Y	NK	23	ST-23 complex	Blood	0.094	0.006	0.008	0.006
38013	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.064	0.006	0.006	0.004
38014	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.064	0.008	0.008	0.004
38015	England	2014/15	B	B	1345	UA	Joint	0.125	0.023	0.008	0.008
38016	England	2014/15	B	B	11484	ST-269 complex	CSF	0.19	0.047	0.006	0.006
38018	Northern Ireland	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.004
38020	England	2014/15	B	B	5151	UA	Blood	0.25	0.016	0.006	0.012
38021	England	2014/15	Y	NK	1655	ST-23 complex	CSF	0.094	0.004	0.008	0.006
38022	England	2014/15	B	B	11486	UA	Blood	0.094	0.023	0.006	0.006
38025	England	2014/15	B	B	11873	ST-41/44 complex	Blood	0.047	0.008	0.006	0.003
38026	England	2014/15	B	B	10696	ST-41/44 complex	Blood	0.19	0.032	0.008	0.008
38028	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.006	0.004
38030	England	2014/15	B	B	8616	ST-269 complex	Blood	0.125	0.004	0.004	0.004
38031	England	2014/15	B	B	485	ST-41/44 complex	Blood	0.19	0.008	0.004	0.006
38033	England	2014/15	B	B	1161	ST-269 complex	CSF	0.064	0.023	0.004	0.004
38036	England	2014/15	B	B	8511	ST-41/44 complex	Blood	0.064	0.016	0.004	0.003
38039	England	2014/15	B	B	11874	ST-41/44 complex	CSF	0.094	0.006	0.004	0.006
38041	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.023	0.004	0.002	0.004
38042	Northern Ireland	2014/15	B	B	1163	ST-269 complex	Blood	0.25	0.006	0.002	0.012
38043	England	2014/15	B	B	1161	ST-269 complex	Blood	0.094	0.004	0.002	0.006
38044	England	2014/15	B	B	485	ST-41/44 complex	Blood	0.19	0.016	0.002	0.008
38045	England	2014/15	B	B	269	ST-269 complex	Blood	0.047	0.006	0.002	0.004
38046	England	2014/15	B	B	1161	ST-269 complex	Blood	0.19	0.012	0.002	0.006
38047	England	2014/15	B	B	11488	ST-213 complex	Blood	0.047	0.008	0.002	0.004
38050	England	2014/15	B	B	11489	ST-213 complex	Blood	0.094	0.012	0.008	0.008
38052	England	2014/15	B	B	154	ST-41/44 complex	CSF	0.047	0.006	0.004	0.004
38053	England	2014/15	Y	NK	11875	ST-23 complex	Blood	0.094	0.003	0.004	0.006
38054	England	2014/15	Y	Y	NK	INCOMPLETE MLST	Joint	0.023	0.002	0.004	0.003
38055	England	2014/15	C	C	2000	ST-32 complex	Blood	0.047	0.016	0.004	0.002
38056	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.004	0.003
38057	England	2014/15	B	B	11893	ST-41/44 complex	Blood	0.047	0.064	0.004	0.003
38058	England	2014/15	B	B	1161	ST-269 complex	Blood	0.064	0.006	0.004	0.004
38061	England	2014/15	W	NK	1617	ST-22 complex	Blood	0.032	0.004	0.004	0.003
38062	England	2014/15	B	B	1575	UA	Blood	0.032	0.006	0.004	0.002
38068	England	2014/15	B	B	3529	ST-269 complex	Blood	0.032	0.008	0.004	0.003
38069	England	2014/15	B	B	1946	ST-461 complex	Blood	0.5	0.016	0.004	0.006
38070	England	2014/15	B	B	11876	ST-461 complex	Blood	0.125	0.004	0.003	0.006
38071	England	2014/15	W/Y	W/Y	3015	UA	Blood	0.094	0.016	0.004	0.004
38072	England	2014/15	B	B	162	ST-162 complex	Blood	0.047	0.023	0.004	0.002
38073	England	2014/15	B	B	269	ST-269 complex	Blood	0.047	0.012	0.004	0.002
38074	England	2014/15	B	B	8758	ST-32 complex	CSF	0.19	0.012	0.004	0.006
38075	England	2014/15	B	B	1161	ST-269 complex	Blood	0.19	0.004	0.004	0.004
38078	England	2014/15	Y	NK	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.004
38080	England	2014/15	B	B	3192	UA	CSF	0.064	0.008	0.002	0.006
38081	Wales	2014/15	B	B	41	ST-41/44 complex	Blood	0.047	0.012	0.004	0.002
38082	England	2014/15	B	B	35	ST-35 complex	Blood	0.125	0.023	0.004	0.002
38083	England	2014/15	B	B	213	ST-213 complex	Blood	0.094	0.016	0.004	0.003
38084	England	2014/15	B	B	213	ST-213 complex	CSF	0.25	0.016	0.004	0.004
38086	England	2014/15	B	B	1946	ST-461 complex	Blood	0.5	0.19	0.004	0.004
38087	England	2014/15	Y	Y	11490	ST-23 complex	Blood	0.064	0.008	0.003	0.004
38089	England	2014/15	B	B	1791	ST-269 complex	Blood	0.064	0.012	0.004	0.003
38090	England	2014/15	B	B	4713	UA	Blood	0.094	0.032	0.004	0.004
38091	England	2014/15	W	NK	1286	ST-22 complex	Blood	0.125	0.012	0.004	0.003

38092	England	2014/15	B	B	7746	ST-41/44 complex	Blood	0.064	0.012	0.002	0.003
38093	England	2014/15	Y	NK	NK	INCOMPLETE MLST	Blood	0.064	0.004	0.004	0.003
38094	England	2014/15	B	B	2203	ST-41/44 complex	Blood	0.064	0.004	0.004	0.003
38095	England	2014/15	B	B	275	ST-269 complex	Blood	0.064	0.006	0.004	0.003
38097	Wales	2014/15	B	B	1096	ST-32 complex	Blood	0.064	0.006	0.004	0.003
38098	England	2014/15	B	B	485	ST-41/44 complex	Blood	0.125	0.004	0.004	0.003
38099	England	2014/15	Y	NK	1655	ST-23 complex	Joint	0.064	0.004	0.004	0.003
38100	England	2014/15	B	B	11227	ST-41/44 complex	CSF	0.19	0.004	0.004	0.004
38103	England	2014/15	B	B	1194	ST-41/44 complex	Blood	0.047	0.008	0.004	0.002
38104	England	2014/15	Y	Y	1655	ST-23 complex	CSF	0.047	0.004	0.004	0.004
38105	England	2014/15	B	B	1161	ST-269 complex	CSF	0.25	0.012	0.004	0.004
38110	England	2014/15	B	B	11492	ST-269 complex	Blood	0.047	0.008	0.004	0.002
38111	England	2014/15	NG	CNL	823	ST-198 complex	Blood	0.19	0.032	0.004	0.004
38112	England	2014/15	B	B	41	ST-41/44 complex	CSF	0.19	0.008	0.004	0.003
38113	England	2014/15	B	B	5151	UA	CSF	0.125	0.004	0.004	0.004
38114	England	2014/15	W/Y	W/Y	167	ST-167 complex	Blood	0.047	0.008	0.004	0.004
38116	England	2014/15	Y	Y	1655	ST-23 complex	Blood	0.032	0.003	0.004	0.003
38117	England	2014/15	B	B	162	ST-162 complex	Blood	0.25	0.023	0.008	0.004
38122	England	2013/14	B	NG	213	ST-213 complex	Blood	0.047	0.032	0.006	0.004
38123	England	2013/14	B	B	213	ST-213 complex	Blood	0.016	0.003	0.004	0.003
38124	England	2013/14	B	B	3120	ST-213 complex	CSF	0.064	0.008	0.006	0.006
38125	Wales	2013/14	B	B	1946	ST-461 complex	Blood	0.25	0.016	0.008	0.008
38129	England	2014/15	Y	NK	1466	ST-174 complex	Blood	0.094	0.004	0.002	0.003
38151	Wales	2014/15	W	W	5121	ST-11 complex	Blood	0.047	0.004	0.004	0.002
39002	England	2014/15	B	B	41	ST-41/44 complex	Blood	0.032	0.012	0.004	0.002
39318	England	2015/16	B	B	11752	UA	Blood	0.047	0.023	0.004	0.003
39319	England	2015/16	C	C	11	ST-11 complex	Blood	0.19	0.032	0.004	0.008
39321	England	2015/16	W/Y	W/Y	1655	ST-23 complex	CSF	0.064	0.004	0.004	0.004
39322	England	2015/16	B	B	269	ST-269 complex	Blood	0.032	0.016	0.002	0.002
39323	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.004	0.004	0.002
39324	England	2015/16	B	B	11753	ST-41/44 complex	Blood	0.094	0.032	0.004	0.004
39325	England	2015/16	B	B	NK	INCOMPLETE MLST	CSF	0.125	0.006	0.004	0.004
39326	Wales	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.004
39327	England	2015/16	W	W	184	ST-22 complex	CSF	0.125	0.012	0.004	0.002
39329	England	2015/16	B	B	4713	UA	Blood	0.064	0.008	0.004	0.003
39330	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.094	0.006	0.004	0.004
39332	Wales	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.008	0.008	0.003
39333	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.125	0.016	0.008	0.002
39334	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.004	0.008	0.003
39336	England	2015/16	B	B	1049	ST-269 complex	Blood	0.047	0.006	0.004	0.002
39338	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.047	0.006	0.004	0.002
39339	England	2015/16	Y	NK	9253	ST-23 complex	Blood	0.25	0.004	0.004	0.004
39343	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.094	0.008	0.008	0.004
39347	England	2015/16	Y	Y	11754	ST-23 complex	Blood	0.047	0.004	0.003	0.004
39348	England	2015/16	B	B	1161	ST-269 complex	Blood	0.094	0.023	0.006	0.008
39350	England	2015/16	B	B	269	ST-269 complex	Blood	0.047	0.006	0.002	0.004
39353	England	2015/16	C	C	11	ST-11 complex	Blood	0.25	0.023	0.004	0.006
39355	England	2015/16	B	B	5151	UA	Blood	0.19	0.006	0.004	0.003
39357	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.25	0.004	0.004	0.004
39360	England	2015/16	B	B	337	ST-41/44 complex	Blood	0.032	0.012	0.004	0.002
39361	England	2015/16	C	C	11	ST-11 complex	Blood	0.38	0.016	0.004	0.008
39362	England	2015/16	B	B	303	ST-41/44 complex	Blood	0.094	0.064	0.008	0.004
39363	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.008	0.003
39364	England	2015/16	B	B	1788	ST-41/44 complex	Blood	0.064	0.008	0.004	0.002
39366	England	2015/16	B	B	485	ST-41/44 complex	CSF	0.25	0.012	0.008	0.006
39367	England	2015/16	B	B	1946	ST-461 complex	Blood	0.5	0.008	0.004	0.006
39370	England	2015/16	B	B	41	ST-41/44 complex	Blood	0.047	0.023	0.008	0.003
39371	England	2015/16	B	B	479	ST-269 complex	Blood	0.25	0.032	0.004	0.006
39372	England	2015/16	B	B	9544	ST-41/44 complex	Blood	0.064	0.008	0.002	0.004
39374	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.125	0.004	0.004	0.004
39375	England	2015/16	B	B	41	ST-41/44 complex	Blood	0.125	0.047	0.004	0.004
39376	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.008	0.006
39377	England	2015/16	Y	Y	1466	ST-174 complex	Blood	0.125	0.094	0.004	0.006
39378	Northern Ireland	2015/16	C	C	11	ST-11 complex	Blood	0.023	0.032	0.008	0.002
39379	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.094	0.016	0.008	0.004
39380	England	2015/16	NG	B	11877	ST-162 complex	Blood	0.5	0.032	0.008	0.023
39381	England	2015/16	B	B	1617	ST-22 complex	Blood	0.064	0.003	0.008	0.004
39382	England	2015/16	B	B	1345	UA	Blood	0.19	0.002	0.004	0.004
39384	England	2015/16	B	B	11238	ST-269 complex	Blood	0.064	0.047	0.008	0.003
39386	England	2015/16	B	B	9088	UA	Blood	0.064	0.003	0.004	0.003
39387	England	2015/16	W	W	1286	ST-22 complex	Blood	0.125	0.004	0.008	0.003
39388	England	2015/16	C	C	11	ST-11 complex	Blood	0.38	0.016	0.008	0.016
39389	England	2015/16	B	B	11756	ST-32 complex	Blood	0.047	0.023	0.008	0.002
39391	England	2015/16	B	B	32	ST-32 complex	Blood	0.25	0.032	0.008	0.006
39392	England	2015/16	B	B	8955	ST-213 complex	Blood	0.047	0.032	0.004	0.004
39393	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.047	0.006	0.008	0.003
39394	England	2015/16	B	B	1194	ST-41/44 complex	Blood	0.047	0.008	0.008	0.003
39397	England	2015/16	B	B	11757	UA	Blood	0.032	0.002	0.004	0.003
39399	England	2015/16	B	B	1161	ST-269 complex	CSF	0.064	0.094	0.004	0.003
39400	England	2015/16	B	B	1194	ST-41/44 complex	CSF	0.19	0.006	0.004	0.004
39402	England	2015/16	B	B	10269	ST-41/44 complex	Blood	0.125	0.012	0.004	0.004
39403	England	2015/16	C	C	11	ST-11 complex	Blood	0.125	0.016	0.004	0.064
39405	Northern Ireland	2015/16	B	B	1157	ST-1157 complex	Blood	0.032	0.012	0.004	0.003
39407	England	2015/16	B	B	409	ST-41/44 complex	Blood	0.38	0.125	0.004	0.008
39409	England	2015/16	C	C	11	ST-11 complex	Blood	0.38	0.032	0.016	0.008

39413	England	2015/16	B	B	4051	UA	BONE MARROW	0.19	0.023	0.004	0.004
39414	Wales	2015/16	B	B	103	ST-103 complex	Blood	0.094	0.016	0.004	0.004
39415	England	2015/16	B	B	34	ST-32 complex	Blood	0.125	0.008	0.004	0.008
39416	England	2015/16	W	W	1281	ST-22 complex	Blood	0.125	0.064	0.004	0.002
39417	England	2015/16	B	B	213	ST-213 complex	Blood	0.064	0.19	0.008	0.003
39418	England	2015/16	B	B	11758	UA	Blood	0.047	0.012	0.004	0.003
39419	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.003
39420	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.004
39422	Wales	2015/16	W	W	11	ST-11 complex	Joint	0.047	0.006	0.004	0.003
39424	England	2015/16	W	W	9316	UA	Blood	0.125	0.023	0.004	0.004
39425	England	2015/16	B	B	1946	ST-461 complex	Blood	0.19	0.008	0.004	0.004
39426	Wales	2015/16	Y	Y	11754	ST-23 complex	CSF	0.064	0.004	0.004	0.004
39432	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.094	0.008	0.008	0.006
39434	England	2015/16	B	B	269	ST-269 complex	Blood	0.094	0.023	0.008	0.003
39437	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.094	0.004	0.008	0.004
39439	England	2015/16	B	B	5440	ST-41/44 complex	Blood	0.094	0.012	0.008	0.004
39440	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.094	0.008	0.004	0.006
40321	Wales	2015/16	B	B	3872	ST-213 complex	Blood	0.38	0.016	0.004	0.008
40324	England	2015/16	B	B	11880	ST-213 complex	CSF	0.38	0.008	0.004	0.004
41452	England	2015/16	B	B	1096	ST-32 complex	Joint	0.064	0.016	0.008	0.004
41453	England	2015/16	B	B	9194	ST-213 complex	Blood	0.094	0.008	0.004	0.003
41454	England	2015/16	B	B	749	ST-32 complex	Blood	0.25	0.008	0.008	0.006
41456	England	2015/16	B	B	1946	ST-461 complex	Blood	0.5	0.012	0.004	0.008
41457	England	2015/16	B	B	275	ST-269 complex	CSF	0.094	0.004	0.004	0.002
41458	Wales	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.002	0.008	0.003
41459	England	2015/16	B	B	10651	ST-11 complex	Blood	0.094	0.008	0.008	0.004
41460	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.5	0.023	0.008	0.008
41461	England	2015/16	B	B	457	ST-35 complex	Blood	0.064	0.004	0.004	0.002
41464	England	2015/16	B	B	303	ST-41/44 complex	Blood	0.38	0.032	0.008	0.008
41465	England	2015/16	B	B	269	ST-269 complex	Blood	0.094	0.012	0.008	0.003
41466	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.125	0.006	0.008	0.004
41468	England	2015/16	C	C	11	ST-11 complex	Blood	0.125	0.008	0.008	0.003
41471	England	2015/16	B	B	485	ST-41/44 complex	Blood	0.38	0.004	0.008	0.004
41472	England	2015/16	C	C	NK	INCOMPLETE MLST	Blood	0.38	0.032	0.008	0.094
41475	England	2015/16	B	B	6058	ST-41/44 complex	Blood	0.19	0.016	0.004	0.004
41476	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.064	0.002	0.004	0.003
41477	England	2015/16	B	B	485	ST-41/44 complex	Blood	0.19	0.004	0.004	0.003
41479	England	2015/16	B	B	4713	UA	Blood	0.125	0.004	0.004	0.003
41480	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.094	0.004	0.004	0.002
41482	England	2015/16	B	B	11917	ST-32 complex	Blood	0.25	0.004	0.004	0.008
41484	England	2015/16	C	C	NK	INCOMPLETE MLST	Blood	0.19	0.032	0.004	0.004
41487	England	2015/16	B	B	1161	ST-269 complex	Blood	0.38	0.008	0.004	0.006
41488	England	2015/16	B	B	4224	ST-213 complex	Blood	0.064	0.008	0.004	0.003
41490	England	2015/16	B	B	5849	UA	Blood	0.125	0.008	0.004	0.004
41491	England	2015/16	B	B	41	ST-41/44 complex	Blood	0.094	0.004	0.004	0.003
41493	England	2015/16	C	C	11	ST-11 complex	Blood	0.38	0.023	0.004	0.008
41495	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.094	0.003	0.004	0.003
41496	England	2015/16	B	B	1161	ST-269 complex	Blood	0.19	0.016	0.006	0.006
41497	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.094	0.003	0.004	0.003
41498	Wales	2015/16	Y	Y	1655	ST-23 complex	Blood	0.094	0.004	0.006	0.004
41499	England	2015/16	Y	NK	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.004
41500	England	2015/16	B	B	213	ST-213 complex	Blood	0.064	0.023	0.004	0.004
41503	England	2015/16	B	B	2713	ST-41/44 complex	Blood	0.047	0.004	0.004	0.003
41504	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.047	0.004	0.004	0.003
41505	England	2015/16	B	B	1194	ST-41/44 complex	Blood	0.047	0.008	0.006	0.004
41506	England	2015/16	B	B	11755	ST-269 complex	Blood	0.25	0.006	0.004	0.006
41507	England	2015/16	B	B	482	ST-41/44 complex	Blood	0.19	0.006	0.006	0.003
41508	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.006
41509	England	2015/16	B	B	7460	ST-32 complex	Blood	0.38	0.012	0.004	0.008
41510	England	2015/16	B	B	7460	ST-32 complex	CSF	0.25	0.016	0.006	0.008
41511	England	2015/16	B	B	6058	ST-41/44 complex	Blood	0.25	0.016	0.006	0.008
41512	England	2015/16	B	B	6359	ST-41/44 complex	Blood	0.19	0.047	0.004	0.003
41513	England	2015/16	B	B	1049	ST-269 complex	Blood	0.047	0.004	0.004	0.003
41514	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.008	0.004	0.003
41517	Wales	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.008	0.002	0.003
41518	England	2015/16	B	B	5534	ST-41/44 complex	Blood	0.19	0.012	0.004	0.004
41520	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.032	0.003	0.004	0.003
41521	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.004
41523	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.023	0.006	0.002	<0.002
41524	England	2015/16	W	W	NK	INCOMPLETE MLST	Joint	0.047	0.008	0.004	0.004
41526	England	2015/16	NG	NG	175	ST-175 complex	Blood	0.19	0.004	0.004	0.004
41529	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.064	0.006	0.004	0.003
41532	Wales	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.094	0.023	0.004	0.003
41534	England	2015/16	Y	Y	1655	ST-23 complex	Joint	0.064	0.004	0.004	0.003
41535	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.064	0.012	0.004	0.004
41537	England	2015/16	B	B	485	ST-41/44 complex	Blood	0.25	0.008	0.004	0.008
41538	England	2015/16	B	B	154	ST-41/44 complex	Blood	0.094	0.004	0.004	0.004
41539	England	2015/16	W	W	1281	ST-22 complex	Blood	0.125	0.016	0.008	0.003
41540	Wales	2015/16	B	B	1161	ST-269 complex	Blood	0.19	0.012	0.008	0.016
41542	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.094	0.016	0.004	0.004
41544	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.25	0.064	0.006	0.006
41545	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.032	0.012	0.008	0.002
41546	Northern Ireland	2015/16	W	W	11	ST-11 complex	CSF	0.047	0.006	0.006	0.004
41548	England	2015/16	B	B	11919	ST-60 complex	Blood	0.19	0.012	0.004	0.003
41550	England	2015/16	B	B	41	ST-41/44 complex	Blood	0.032	0.012	0.004	<0.002

41551	England	2015/16	Y	Y	1466	ST-174 complex	Blood	0.125	0.016	0.003	0.006
41553	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
41554	England	2015/16	B	B	485	ST-41/44 complex	Blood	0.19	0.006	0.006	0.004
41555	England	2015/16	B	B	60	ST-60 complex	Blood	0.047	0.023	0.004	0.002
41556	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.094	0.004	0.004	0.004
41557	England	2015/16	Y	Y	1655	ST-23 complex	CSF	0.064	0.008	0.004	0.004
41559	England	2015/16	B	B	485	ST-41/44 complex	Blood	0.25	0.016	0.006	0.006
42473	Northern Ireland	2015/16	B	B	32	ST-32 complex	Blood	0.25	0.006	0.004	0.004
42474	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.094	0.004	0.004	0.004
42477	England	2015/16	B	B	12173	ST-41/44 complex	Blood	0.25	0.006	0.004	0.004
42479	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.003
42487	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.047	0.008	0.003	0.004
42488	England	2015/16	B	B	1161	ST-269 complex	Blood	0.064	0.012	0.006	0.006
42490	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.094	0.004	0.004	0.004
42493	England	2015/16	W	NK	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.002
42496	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.004
42498	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.032	0.004	0.003	<0.002
42499	England	2015/16	C	C	NK	INCOMPLETE MLST	Blood	0.19	0.5	0.004	0.094
42500	England	2015/16	W/Y	W/Y	NK	INCOMPLETE MLST	Blood	0.032	0.004	0.004	0.003
42501	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.25	0.016	0.004	0.006
42502	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.047	0.004	0.004	0.004
42507	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.006	0.004	0.006
42508	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.094	0.016	0.006	0.006
42509	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.125	0.047	0.004	<0.002
42510	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.047	0.006	0.004	0.006
42511	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.064	0.006	0.004	0.003
42513	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.19	0.006	0.004	0.012
42514	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.125	0.008	0.004	0.004
42515	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.003	0.004	0.003
42516	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.003	0.004	0.003
42518	England	2015/16	Y	Y	12176	ST-23 complex	Blood	0.047	0.003	0.004	0.004
42520	England	2015/16	B	B	12017	UA	Blood	0.023	<0.002	0.003	0.003
42521	England	2015/16	B	B	213	ST-213 complex	Blood	0.047	0.006	0.004	0.002
42522	England	2015/16	B	B	2314	ST-41/44 complex	Blood	0.094	0.004	0.004	0.004
42523	England	2015/16	B	B	1791	ST-269 complex	CSF	0.064	0.032	0.004	0.006
42524	England	2015/16	C	C	11	ST-11 complex	Blood	0.064	0.008	0.004	0.006
42527	Wales	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.006
42528	Wales	2015/16	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.004	0.003
42529	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.004
42531	England	2015/16	B	B	11466	ST-269 complex	Blood	0.032	0.012	0.004	0.002
42536	England	2015/16	B	B	269	ST-269 complex	Blood	0.064	0.008	0.004	0.003
42538	Northern Ireland	2015/16	Y	NK	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.006
42539	England	2015/16	Y	Y	3582	ST-23 complex	Blood	0.125	0.008	0.004	0.008
42540	England	2015/16	C	C	11	ST-11 complex	Blood	0.38	0.047	0.004	0.012
42541	England	2015/16	C	C	11	ST-11 complex	Blood	0.38	0.008	0.004	0.006
42542	England	2015/16	B	B	9194	ST-213 complex	Blood	0.047	0.012	0.004	<0.002
42543	England	2015/16	Y	NK	5436	UA	Blood	0.064	0.023	0.004	0.004
42544	England	2015/16	B	B	8988	UA	Blood	0.25	0.125	0.008	0.004
42546	England	2015/16	B	B	213	ST-213 complex	Joint	0.25	0.008	0.004	0.006
42547	Wales	2015/16	B	B	1946	ST-461 complex	Blood	0.25	0.023	0.004	0.006
42548	England	2015/16	B	B	1161	ST-269 complex	Blood	0.125	0.006	0.004	0.004
42550	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.006	0.004	0.003
42554	England	2015/16	B	B	2166	ST-269 complex	CSF	0.064	0.012	0.004	0.002
42557	England	2015/16	Y	NK	23	ST-23 complex	Blood	0.094	<0.002	0.003	0.003
42558	England	2015/16	B	B	8273	UA	Blood	0.047	0.016	0.004	0.002
42559	England	2015/16	C	C	11	ST-11 complex	Blood	0.064	0.012	0.006	0.004
42560	England	2015/16	B	B	1161	ST-269 complex	Blood	0.094	0.008	0.004	0.003
42562	England	2015/16	B	B	1096	ST-32 complex	Blood	0.064	0.047	0.004	0.004
42563	England	2015/16	B	B	461	ST-461 complex	Blood	0.25	0.016	0.004	0.004
42565	England	2015/16	B	B	6058	ST-41/44 complex	Blood	0.19	0.047	0.004	0.004
42566	England	2015/16	C	C	12020	ST-103 complex	Blood	0.125	0.016	0.004	0.003
42567	England	2015/16	B	B	12011	ST-213 complex	Blood	0.25	0.016	0.004	0.004
42569	Northern Ireland	2015/16	C	C	NK	INCOMPLETE MLST	Blood	0.094	0.023	0.008	0.006
42571	England	2015/16	B	B	571	ST-41/44 complex	Blood	0.064	0.012	0.004	0.004
42574	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.047	0.016	0.004	0.003
42575	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.012	0.004	0.003
42577	England	2015/16	C	C	11	ST-11 complex	Blood	0.047	0.032	0.004	0.003
42578	England	2015/16	C	C	NK	INCOMPLETE MLST	Blood	0.25	0.016	0.004	0.006
42579	England	2015/16	B	B	275	ST-269 complex	Blood	0.064	0.064	0.004	0.004
42580	England	2015/16	B	B	1111	UA	Blood	0.38	0.032	0.004	0.032
42581	England	2015/16	C	C	11	ST-11 complex	Blood	0.094	0.016	0.004	0.006
42582	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.125	0.016	0.003	0.006
42583	England	2015/16	B	B	213	ST-213 complex	Blood	0.047	0.012	0.004	0.004
42584	England	2015/16	B	B	12174	ST-461 complex	CSF	0.25	0.008	0.004	0.006
42587	Wales	2015/16	B	B	41	ST-41/44 complex	Joint	0.047	0.006	0.004	<0.002
42588	England	2015/16	B	B	41	ST-41/44 complex	Blood	0.19	0.008	0.004	0.004
42589	England	2015/16	B	B	162	ST-162 complex	Blood	0.064	0.016	0.004	0.004
42590	Wales	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.047	0.004	0.004	0.003
42591	England	2015/16	B	B	275	ST-269 complex	Blood	0.064	0.004	0.004	0.003
42592	Wales	2015/16	B	B	1090	ST-41/44 complex	Blood	0.19	0.008	0.004	0.003
42593	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.047	0.004	0.004	0.003
42594	England	2015/16	B	B	1194	ST-41/44 complex	Blood	0.125	0.008	0.006	0.006
42596	England	2015/16	Y	Y	10730	ST-167 complex	Blood	0.094	0.003	0.004	0.008
42597	England	2015/16	C	C	11	ST-11 complex	Blood	0.25	0.047	0.004	0.008
42598	Northern Ireland	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.25	0.012	0.006	0.004

42599	Wales	2015/16	Y	NK	23	ST-23 complex	Blood	0.125	0.002	0.004	0.004
42600	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.003	0.004
42601	England	2015/16	B	B	12177	ST-32 complex	Blood	0.064	0.064	0.004	0.003
42602	England	2015/16	B	B	213	ST-213 complex	Blood	0.064	0.012	0.004	0.002
42603	England	2015/16	B	B	1054	UA	Blood	0.19	0.064	0.004	0.003
42604	England	2015/16	B	B	12178	ST-213 complex	Blood	0.032	0.006	0.004	0.003
42606	Wales	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.008	0.008	0.004
42607	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.004
42608	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.003
42609	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.008	0.004
42610	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.008	0.004	0.004
42611	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.012	0.004	0.004
42613	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.125	0.004	0.004	0.008
42614	England	2015/16	Y	Y	3015	UA	Blood	0.047	0.012	0.004	0.004
42615	England	2015/16	C	C	11	ST-11 complex	Blood	0.064	0.012	0.004	0.003
44635	England	2015/16	B	B	749	ST-32 complex	Blood	0.19	0.006	0.004	<0.002
44637	England	2015/16	B	B	41	ST-41/44 complex	Blood	0.25	0.006	0.004	0.006
44639	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.094	0.008	0.004	0.004
44641	England	2015/16	B	B	41	ST-41/44 complex	Blood	0.047	0.012	0.003	0.004
44696	England	2015/16	B	B	213	ST-213 complex	Blood	0.25	0.047	0.004	0.004
44698	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.004	0.004	0.003
44700	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.25	0.006	0.006	0.006
44701	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.008	0.004	0.004
44702	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.064	0.008	0.008	0.004
44703	England	2015/16	B	B	1161	ST-269 complex	Blood	0.19	0.006	0.004	0.003
44705	England	2015/16	B	B	11395	ST-32 complex	Blood	0.38	0.008	0.004	0.004
44706	England	2015/16	Y	Y	11754	ST-23 complex	Blood	0.19	0.008	0.006	0.006
44707	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.008	0.004	0.004
44709	England	2015/16	C	C	5133	ST-103 complex	Blood	0.064	0.012	0.004	0.003
44710	England	2015/16	B	B	12345	ST-32 complex	Blood	0.25	0.004	0.002	0.004
44711	England	2015/16	B	B	269	ST-269 complex	CSF	0.25	0.008	0.004	<0.002
44713	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.094	0.004	0.004	0.004
44715	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.25	0.064	0.004	0.006
44716	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.023	0.004	0.004
44717	Northern Ireland	2015/16	B	B	213	ST-213 complex	Blood	0.094	0.023	0.004	0.006
44720	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.006	0.006
44722	Wales	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.004	0.004	0.006
44723	England	2015/16	B	B	1157	ST-1157 complex	Blood	0.19	0.004	0.004	0.004
44725	Northern Ireland	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
44726	England	2015/16	W	W	22	ST-22 complex	Blood	0.125	0.008	0.004	<0.002
44728	England	2015/16	C	C	11	ST-11 complex	Blood	0.094	0.008	0.008	0.006
44729	England	2015/16	B	B	354	ST-269 complex	Blood	0.064	0.006	0.006	0.003
44732	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.094	0.006	0.004	0.004
44734	England	2015/16	B	B	9316	UA	Blood	0.125	0.008	0.004	0.006
44735	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.094	0.006	0.006	0.004
44737	England	2015/16	B	B	269	ST-269 complex	Blood	0.047	0.008	0.006	0.002
44738	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.125	0.008	0.008	0.006
44741	England	2015/16	C	C	11	ST-11 complex	Blood	0.047	0.016	0.004	<0.002
44743	England	2015/16	B	B	NK	INCOMPLETE MLST	CSF	0.125	0.012	0.008	0.004
44744	England	2015/16	B	B	12215	ST-41/44 complex	Blood	0.19	0.008	0.004	0.006
44745	England	2015/16	B	B	485	ST-41/44 complex	Blood	0.125	0.008	0.008	0.003
44747	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.094	0.006	0.004	0.006
44748	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.094	0.004	0.004	0.004
44749	England	2015/16	B	B	12011	ST-213 complex	Blood	0.25	0.008	0.002	<0.002
44750	Wales	2015/16	B	B	1097	ST-41/44 complex	Blood	0.064	0.012	<0.002	0.004
44751	England	2015/16	Y	Y	23	ST-23 complex	CSF	0.094	0.008	0.002	0.004
44752	England	2015/16	B	B	41	ST-41/44 complex	Blood	0.064	0.032	0.003	0.004
44756	England	2015/16	B	B	2660	ST-213 complex	CSF	0.094	0.064	0.004	<0.002
44757	England	2015/16	B	B	NK	INCOMPLETE MLST	CSF	0.25	0.012	0.004	0.003
44758	England	2015/16	B	B	12224	ST-22 complex	Blood	0.38	0.125	0.004	0.004
44760	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.047	0.003	0.004	<0.002
44761	England	2015/16	Y	Y	114	ST-22 complex	Blood	0.125	0.008	0.006	0.004
44762	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.125	0.032	0.004	0.004
44764	England	2015/16	B	B	8021	ST-213 complex	CSF	0.125	0.023	0.004	0.003
44766	England	2015/16	B	B	1163	ST-269 complex	Blood	0.064	0.012	0.004	<0.002
44767	Wales	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.004	0.004	0.004
44770	England	2015/16	C	C	11	ST-11 complex	Joint	0.19	0.006	0.004	0.004
44771	England	2015/16	B	B	461	ST-461 complex	Blood	0.125	0.047	0.004	0.003
44772	England	2015/16	B	B	162	ST-162 complex	Blood	0.125	0.023	0.008	0.004
44774	England	2015/16	B	B	275	ST-269 complex	Blood	0.125	0.023	0.004	0.003
44775	England	2015/16	Y	NK	1655	ST-23 complex	Blood	0.094	0.006	0.004	0.003
44776	England	2015/16	B	B	1161	ST-269 complex	Blood	0.38	0.023	0.004	0.004
44778	England	2015/16	B	B	12226	ST-461 complex	Blood	0.25	0.064	0.004	0.004
44779	England	2015/16	C	C	11	ST-11 complex	Blood	0.125	0.016	0.004	0.004
44780	England	2015/16	B	B	1195	ST-269 complex	Blood	0.032	0.008	0.004	0.002
44781	England	2015/16	B	B	41	ST-41/44 complex	Blood	0.19	0.003	0.004	0.003
44783	Wales	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.094	0.006	0.004	0.004
44787	England	2015/16	B	B	7460	ST-32 complex	Blood	0.25	0.012	0.002	0.008
44789	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Joint	0.047	0.006	0.004	0.003
44791	England	2015/16	B	B	60	ST-60 complex	CSF	0.047	0.004	0.006	0.003
44792	England	2015/16	C	C	NK	INCOMPLETE MLST	Blood	0.19	0.012	0.004	0.006
44793	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.004	<0.002
44794	England	2015/16	B	B	41	ST-41/44 complex	Blood	0.032	0.008	0.004	<0.002
44796	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.047	0.006	0.004	0.003
44797	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.047	0.064	0.003	0.004

44799	England	2015/16	C	C	NK	INCOMPLETE MLST	Blood	0.125	0.004	0.003	0.006
44800	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.125	0.006	0.006	0.008
44801	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.008	0.008	0.006
44803	England	2015/16	B	B	275	ST-269 complex	Blood	0.047	0.023	0.006	0.003
44804	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.125	0.047	0.006	0.012
44805	England	2015/16	E	E	NK	INCOMPLETE MLST	Blood	0.094	0.125	0.006	0.006
44806	England	2015/16	C	C	12227	ST-11 complex	Blood	0.047	0.125	0.006	0.003
44807	England	2015/16	B	B	41	ST-41/44 complex	Blood	0.19	0.023	0.006	0.006
44808	England	2015/16	B	B	41	ST-41/44 complex	Blood	0.064	0.064	0.004	0.003
44809	Wales	2015/16	B	B	41	ST-41/44 complex	Blood	0.032	0.012	0.004	<0.002
44810	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.094	0.023	0.004	0.008
44811	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.5	0.016	0.004	0.047
44812	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.25	0.016	0.008	0.006
44813	England	2015/16	B	B	11238	ST-269 complex	Blood	0.064	0.032	0.006	0.004
44814	England	2015/16	Y	Y	23	ST-23 complex	Blood	0.064	0.004	0.004	0.004
44815	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.25	0.032	0.006	0.008
44816	England	2015/16	B	B	12237	UA	Blood	0.047	0.032	0.006	0.003
44817	England	2015/16	Y	Y	1625	ST-23 complex	Blood	0.19	0.006	0.004	0.023
44818	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.047	0.003	0.004	0.002
44819	England	2015/16	B	B	461	ST-461 complex	Blood	0.25	0.012	0.004	0.006
44820	Northern Ireland	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.016	0.008	0.004
44821	England	2015/16	B	B	1159	UA	Blood	0.032	0.023	0.004	0.004
44822	England	2015/16	Y	Y	1655	ST-23 complex	Joint	0.064	0.004	0.006	0.003
44823	England	2015/16	B	B	5849	UA	Blood	0.094	0.008	0.006	0.004
44824	England	2015/16	B	B	11	ST-11 complex	Blood	0.38	0.25	0.004	0.012
44825	England	2015/16	B	B	1163	ST-269 complex	CSF	0.094	0.047	0.004	0.004
44826	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.047	0.016	0.006	0.002
44827	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.25	0.008	0.006	0.004
44830	England	2015/16	B	B	12346	UA	Blood	0.023	0.012	0.004	<0.002
44831	England	2015/16	B	B	NK	INCOMPLETE MLST	CSF	0.047	0.012	0.004	0.003
44834	England	2015/16	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.064	0.008	0.008
44836	England	2015/16	Y	Y	NK	INCOMPLETE MLST	Blood	0.064	0.004	0.004	0.004
47017	England	2015/16	B	B	3446	ST-41/44 complex	Blood	0.064	0.004	0.008	0.003
47018	England	2015/16	B	B	1161	ST-269 complex	Blood	0.25	0.023	0.003	0.004
47259	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.004	0.003
47260	England	2015/16	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.004
47261	England	2015/16	B	B	1403	ST-41/44 complex	Blood	0.032	0.012	0.002	0.004
47264	England	2015/16	Y	Y	10730	ST-167 complex	Blood	0.094	0.006	0.004	0.006
47266	England	2015/16	C	C	11	ST-11 complex	Blood	0.064	0.016	0.006	0.008
47267	England	2015/16	B	B	1161	ST-269 complex	Blood	0.125	0.012	0.008	0.002
47268	England	2015/16	B	B	1161	ST-269 complex	Blood	0.38	0.023	0.006	0.008
47269	England	2016/17	B	B	162	ST-162 complex	Blood	0.38	0.016	0.004	0.008
47270	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.19	0.012	0.008	0.012
47272	England	2016/17	B	B	162	ST-162 complex	Blood	0.064	0.008	0.004	0.003
47276	England	2016/17	B	B	1788	ST-41/44 complex	CSF	0.064	0.006	0.004	0.002
47278	Wales	2016/17	B	B	2314	ST-41/44 complex	Blood	0.125	0.004	0.004	0.004
47279	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.064	0.012	0.004	0.004
47281	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.004
47282	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.006
47283	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.004
47284	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.002
47285	England	2016/17	B	B	1161	ST-269 complex	Blood	0.125	0.008	0.008	0.006
47286	England	2016/17	B	B	1195	ST-269 complex	Blood	0.125	0.012	0.008	0.006
47288	Wales	2016/17	B	B	1092	ST-269 complex	CSF	0.064	0.008	0.004	0.003
47290	England	2016/17	NG	CNL	12513	ST-198 complex	Blood	0.125	0.19	0.004	0.006
47291	England	2016/17	B	B	12509	ST-32 complex	Blood	0.25	0.016	0.006	0.008
47292	England	2016/17	B	B	1946	ST-461 complex	Blood	0.25	0.012	0.004	0.006
47295	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.094	0.012	0.006	0.006
47297	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.25	0.016	0.004	0.004
47298	England	2016/17	C	C	11	ST-11 complex	CSF	0.094	0.012	0.008	0.006
47300	England	2016/17	B	B	34	ST-32 complex	Blood	0.19	0.006	0.006	0.012
47302	England	2016/17	Y	NK	1655	ST-23 complex	Blood	0.094	0.006	0.004	0.003
47306	England	2016/17	B	B	2380	ST-35 complex	Blood	0.094	0.012	0.008	0.003
47307	England	2016/17	B	B	1098	ST-32 complex	CSF	0.38	0.032	0.004	0.004
47308	England	2016/17	C	C	11	ST-11 complex	Blood	0.38	0.064	0.008	0.006
47309	England	2016/17	B	B	275	ST-269 complex	Blood	0.25	0.012	0.006	0.003
47310	England	2016/17	B	B	336	UA	Blood	0.25	0.006	0.006	0.006
47312	England	2016/17	B	B	3641	ST-213 complex	Blood	0.125	0.023	0.004	0.008
47313	England	2016/17	W	W	1617	ST-22 complex	Blood	0.38	0.004	0.004	0.008
47314	England	2016/17	B	B	1194	ST-41/44 complex	Blood	0.25	0.004	0.004	0.004
47315	England	2016/17	Y	Y	1655	ST-23 complex	Joint	0.047	0.004	0.004	0.003
47316	England	2016/17	Y	Y	23	ST-23 complex	Blood	0.094	0.004	0.004	0.004
47317	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.064	0.012	0.004	0.003
47319	England	2016/17	B	B	1111	UA	Blood	0.38	0.125	0.004	0.003
47320	England	2016/17	Y	Y	23	ST-23 complex	CSF	0.19	0.008	0.008	0.006
47321	Wales	2016/17	B	B	5133	ST-103 complex	Blood	0.032	0.023	0.004	0.002
47323	England	2016/17	B	B	571	ST-41/44 complex	CSF	0.064	0.006	0.004	0.003
47324	England	2016/17	Y	Y	23	ST-23 complex	Blood	0.094	0.004	0.004	0.006
47328	Wales	2016/17	B	B	8049	ST-32 complex	Blood	0.38	0.016	0.004	0.004
47330	England	2016/17	Y	NK	1655	ST-23 complex	Blood	0.125	0.004	0.004	0.004
47331	England	2016/17	B	B	12510	UA	Blood	0.125	0.047	0.008	0.006
47332	England	2016/17	B	B	12510	UA	Blood	0.125	0.047	0.006	0.006
47333	England	2016/17	B	B	12512	ST-41/44 complex	Blood	0.125	0.016	0.004	0.006
47335	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.094	0.008	0.004	0.003
47339	England	2016/17	C	C	11	ST-11 complex	Blood	0.047	0.047	0.004	0.004

47341	England	2016/17	B	B	9316	UA	Blood	0.125	0.064	0.004	0.003
47342	England	2016/17	B	B	11466	ST-269 complex	Blood	0.047	0.016	0.004	0.003
47343	England	2016/17	W	W	184	ST-22 complex	Blood	0.125	0.008	0.004	0.003
53052	Wales	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.003
53055	England	2016/17	Y	Y	10728	ST-167 complex	Blood	0.19	0.006	0.008	0.012
53057	England	2016/17	B	B	8988	UA	Blood	0.19	0.032	0.008	0.006
53059	England	2016/17	B	B	340	ST-41/44 complex	Blood	0.125	0.006	0.004	0.004
53061	England	2016/17	Y	Y	23	ST-23 complex	Blood	0.064	0.006	0.004	0.002
53062	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.003
53063	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.064	0.125	0.008	0.003
53065	England	2016/17	B	B	485	ST-41/44 complex	Blood	0.19	0.047	0.004	0.004
53066	England	2016/17	Y	Y	23	ST-23 complex	Blood	0.38	0.012	0.004	0.023
53068	England	2016/17	B	B	12985	ST-213 complex	Blood	0.25	0.008	0.004	0.003
53070	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.19	0.008	0.004	0.006
53071	Wales	2016/17	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.004	0.002
53073	England	2016/17	B	B	13091	ST-60 complex	Blood	0.125	0.012	0.004	0.004
53075	England	2016/17	B	B	1161	ST-269 complex	Blood	0.19	0.006	0.004	0.006
53079	England	2016/17	W/Y	W/Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.003
53083	England	2016/17	B	B	269	ST-269 complex	CSF	0.047	0.008	0.004	0.002
53085	England	2016/17	Y	Y	13092	ST-23 complex	Blood	0.047	0.003	0.004	0.003
53088	England	2016/17	C	C	11	ST-11 complex	Blood	0.064	0.004	0.004	0.004
53089	England	2016/17	C	C	11	ST-11 complex	Joint	0.047	0.016	0.004	0.004
53090	England	2016/17	C	C	11	ST-11 complex	Blood	0.25	0.012	0.004	0.004
53094	England	2016/17	B	B	457	ST-35 complex	Blood	0.032	0.032	0.004	<0.002
53095	England	2016/17	C	C	11	ST-11 complex	CSF	0.064	0.023	0.004	0.003
53097	England	2016/17	B	B	1774	ST-269 complex	Blood	0.125	0.023	0.004	0.003
53098	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.002
53099	England	2016/17	B	B	13095	ST-32 complex	Blood	0.19	0.003	0.004	0.004
53100	England	2016/17	C	C	11	ST-11 complex	Blood	0.125	0.016	0.004	0.003
53101	England	2016/17	B	B	213	ST-213 complex	Blood	0.19	0.012	0.004	0.006
53102	England	2016/17	B	B	1475	ST-41/44 complex	Blood	0.047	0.094	0.004	0.003
53103	Wales	2016/17	Y	Y	23	ST-23 complex	Blood	0.125	0.003	0.003	0.004
53104	England	2016/17	B	B	1162	UA	Blood	0.032	0.064	0.004	0.002
53105	England	2016/17	C	C	11	ST-11 complex	Blood	0.094	0.016	0.004	0.006
53106	England	2016/17	Y	Y	13093	ST-23 complex	Blood	0.094	0.004	0.004	0.008
53107	England	2016/17	B	B	485	ST-41/44 complex	Blood	0.125	0.006	0.004	0.003
53108	England	2016/17	Y	Y	1655	ST-23 complex	Joint	0.064	0.006	0.004	0.003
53109	England	2016/17	B	B	10266	UA	Blood	0.38	0.008	0.004	0.012
53111	England	2016/17	B	B	1423	ST-41/44 complex	Blood	0.047	0.008	0.004	0.003
53112	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.006
53114	England	2016/17	B	B	32	ST-32 complex	Blood	0.047	0.008	0.004	0.004
53115	England	2016/17	B	B	1992	ST-41/44 complex	CSF	0.125	0.004	0.004	0.003
53116	England	2016/17	B	B	4146	ST-60 complex	Blood	0.032	0.032	0.008	0.002
53117	England	2016/17	B	B	1475	ST-41/44 complex	Joint	0.064	0.006	0.004	0.003
53118	England	2016/17	B	B	1161	ST-269 complex	Blood	0.032	0.016	0.004	0.008
53120	Wales	2016/17	B	B	12987	UA	Blood	0.047	0.023	0.008	0.004
53122	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.003
53124	Wales	2016/17	B	B	269	ST-269 complex	Blood	0.064	0.047	0.004	0.004
53125	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.012	0.004	0.003
53126	England	2016/17	B	B	3754	ST-41/44 complex	Blood	0.032	0.004	0.008	0.003
53127	England	2016/17	B	B	409	ST-41/44 complex	Blood	0.125	0.064	0.004	0.006
53128	England	2016/17	B	B	485	ST-41/44 complex	Blood	0.19	0.016	0.004	0.004
53129	England	2016/17	B	B	13094	ST-41/44 complex	Blood	0.047	0.012	0.004	0.002
53130	England	2016/17	B	B	283	ST-269 complex	Blood	0.047	0.008	0.004	0.003
53131	England	2016/17	B	B	11	ST-11 complex	Blood	0.064	0.012	0.004	0.006
53132	England	2016/17	B	B	34	ST-32 complex	Blood	0.19	0.006	0.004	0.006
53134	England	2016/17	B	B	13096	ST-32 complex	Blood	0.047	0.006	0.004	0.004
53136	England	2016/17	B	B	12988	UA	CSF	0.064	0.004	0.004	0.004
53137	England	2016/17	B	B	34	ST-32 complex	Blood	0.125	0.006	0.004	0.012
53138	England	2016/17	B	B	1049	ST-269 complex	Blood	0.064	0.016	0.004	0.003
53140	England	2016/17	B	B	8988	UA	Blood	0.125	0.012	0.004	0.003
53144	Wales	2016/17	B	B	12989	ST-269 complex	Blood	0.032	0.008	0.004	0.002
53145	Wales	2016/17	B	B	41	ST-41/44 complex	Blood	0.032	0.006	0.004	0.002
53147	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.004
53148	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.125	0.008	0.004	0.004
53152	England	2016/17	B	B	32	ST-32 complex	Blood	0.19	0.012	0.004	0.006
53153	England	2016/17	B	B	8511	ST-41/44 complex	Blood	0.047	0.004	0.004	0.003
53155	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.003
53156	Wales	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.032	0.004	0.004
53157	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.19	0.008	0.004	0.006
53158	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.004
53160	England	2016/17	C	C	12227	ST-11 complex	Blood	0.047	0.032	0.004	0.004
53161	England	2016/17	B	B	3482	UA	Blood	0.047	0.19	0.004	0.003
53162	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.064	0.008	0.004	0.004
53163	England	2016/17	B	B	749	ST-32 complex	Blood	0.125	0.008	0.004	0.006
53168	Wales	2016/17	W	NK	11	ST-11 complex	Blood	0.064	0.012	0.008	0.003
53169	England	2016/17	B	B	1049	ST-269 complex	Blood	0.032	0.006	0.008	0.002
53171	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
53172	Northern Ireland	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.023	0.004	0.003
53173	England	2016/17	B	B	18	ST-18 complex	Blood	0.012	0.002	0.008	0.002
53174	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.003
53175	England	2016/17	B	B	485	ST-41/44 complex	Blood	0.094	0.006	0.008	0.004
53177	England	2016/17	B	B	1049	ST-269 complex	Blood	0.023	0.006	0.008	0.002
53180	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.008	0.006
53181	England	2016/17	B	B	34	ST-32 complex	Blood	0.19	0.008	0.004	0.006

53182	England	2016/17	B	B	162	ST-162 complex	Blood	0.032	0.023	0.008	0.002
53184	England	2016/17	B	B	485	ST-41/44 complex	Blood	0.125	0.016	0.008	0.003
53185	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.094	0.012	0.004	0.003
53186	England	2016/17	B	B	269	ST-269 complex	Blood	0.047	0.006	0.008	0.003
53187	England	2016/17	B	B	162	ST-162 complex	Blood	0.047	0.012	0.008	0.004
53189	England	2016/17	B	B	1161	ST-269 complex	Blood	0.047	0.016	0.004	0.003
53191	England	2016/17	B	B	12990	UA	Blood	0.032	0.003	0.008	0.002
53193	England	2016/17	C	C	11	ST-11 complex	Blood	0.032	0.012	0.008	0.003
53197	England	2016/17	B	B	2314	ST-41/44 complex	Blood	0.094	0.006	0.004	0.003
53201	England	2016/17	Y	Y	23	ST-23 complex	Blood	0.032	0.002	0.004	0.003
53202	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.032	0.003	0.004	0.003
53203	England	2016/17	Y	Y	1655	ST-23 complex	Joint	0.047	0.004	0.004	0.004
53204	England	2016/17	B	B	162	ST-162 complex	Blood	0.25	0.012	0.008	0.008
53205	England	2016/17	Y	Y	6463	ST-23 complex	Blood	0.094	0.006	0.004	0.008
53206	England	2016/17	B	B	1721	ST-213 complex	Blood	0.032	0.012	0.008	0.003
53209	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.047	0.008	0.008	0.003
53210	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.125	0.004	0.008	0.004
53211	England	2016/17	Y	Y	23	ST-23 complex	Blood	0.032	0.006	0.004	0.003
53214	England	2016/17	C	C	11	ST-11 complex	Blood	0.125	0.016	0.008	0.004
53216	England	2016/17	B	B	13098	ST-213 complex	Blood	0.016	0.004	0.004	<0.002
53218	Wales	2016/17	Y	Y	23	ST-23 complex	Blood	0.047	0.002	0.004	0.003
53219	England	2016/17	B	B	461	ST-461 complex	CSF	0.125	0.004	0.004	0.004
53220	England	2016/17	Y	Y	23	ST-23 complex	Blood	0.5	0.032	0.004	0.006
53221	Wales	2016/17	W	W	11	ST-11 complex	CSF	0.047	0.004	0.004	0.003
53223	Wales	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.006	0.008	0.003
53224	Wales	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.016	0.008	0.003
53225	England	2016/17	B	B	213	ST-213 complex	Blood	0.032	0.016	0.008	0.008
53227	England	2016/17	Y	Y	23	ST-23 complex	Blood	0.032	0.006	0.004	0.003
53228	England	2016/17	B	B	1946	ST-461 complex	Blood	0.25	0.023	0.004	0.006
53229	England	2016/17	B	B	5266	ST-269 complex	Blood	0.023	0.004	0.008	0.002
53234	England	2016/17	B	B	467	ST-269 complex	Blood	0.125	0.047	0.004	0.004
53235	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.008	0.002
53238	England	2016/17	B	B	1161	ST-269 complex	Blood	0.064	0.004	0.008	0.004
53239	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.003
53240	England	2016/17	B	B	213	ST-213 complex	Blood	0.047	0.004	0.004	0.002
53241	England	2016/17	B	B	2314	ST-41/44 complex	CSF	0.094	0.012	0.008	0.004
53242	England	2016/17	B	B	33	ST-32 complex	Joint	0.047	0.003	0.008	0.002
53243	England	2016/17	B	B	1163	ST-269 complex	Blood	0.094	0.006	0.004	0.002
53245	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.023	0.002	0.004	0.003
53247	England	2016/17	B	B	2561	ST-269 complex	Blood	0.094	0.023	0.004	0.004
53248	England	2016/17	B	B	11766	ST-41/44 complex	Blood	0.023	0.003	0.004	0.002
53250	Northern Ireland	2016/17	B	B	269	ST-269 complex	Blood	0.023	0.023	0.008	0.003
53251	England	2016/17	Y	Y	11520	UA	Blood	0.094	0.004	0.008	0.004
53254	England	2016/17	B	B	467	ST-269 complex	Blood	0.38	0.19	0.008	0.012
53257	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.008	0.004
53258	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.008	0.004
53260	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.25	0.006	0.008	0.003
53261	England	2016/17	Y	Y	1624	ST-167 complex	Blood	0.125	0.003	0.008	0.012
53262	England	2016/17	C	C	11	ST-11 complex	Blood	0.064	0.012	0.008	0.006
53263	England	2016/17	B	B	1161	ST-269 complex	Blood	0.047	0.008	0.004	0.003
53266	England	2016/17	B	B	11480	UA	Blood	0.094	0.004	0.004	0.006
53268	England	2016/17	W	W	9316	UA	Blood	0.094	0.023	0.004	0.003
53271	England	2016/17	B	B	7746	ST-41/44 complex	Blood	0.032	0.004	0.008	0.002
53272	England	2016/17	Y	Y	3015	UA	Blood	0.094	0.016	0.004	0.004
53273	England	2016/17	B	B	485	ST-41/44 complex	Blood	0.125	0.003	0.008	0.004
53276	England	2016/17	C	C	11	ST-11 complex	CSF	0.047	0.002	0.004	0.002
53277	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.032	0.002	0.004	0.003
53278	Northern Ireland	2016/17	C	C	11	ST-11 complex	Blood	0.016	<0.002	0.004	0.002
53280	England	2016/17	C	C	11	ST-11 complex	Blood	0.064	0.064	0.004	0.004
53281	England	2016/17	B	B	32	ST-32 complex	Blood	0.032	0.016	0.004	0.002
53282	England	2016/17	B	B	1867	UA	Blood	0.047	0.008	0.004	0.004
53283	England	2016/17	Y	Y	23	ST-23 complex	Blood	0.047	0.012	0.002	0.004
53285	England	2016/17	B	B	12509	ST-32 complex	Blood	0.125	0.008	0.004	0.006
53286	England	2016/17	B	B	12991	ST-269 complex	Blood	0.125	0.047	0.004	0.004
53288	England	2016/17	B	B	2314	ST-41/44 complex	Blood	0.094	0.064	0.004	0.003
53289	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.016	0.002	0.004	<0.002
53290	England	2016/17	B	B	12227	ST-11 complex	Blood	0.032	0.023	0.004	0.002
53293	England	2016/17	B	B	11466	ST-269 complex	Blood	0.064	0.008	0.008	0.002
53294	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.004	0.003
53295	England	2016/17	B	B	4562	ST-213 complex	Blood	0.094	0.023	0.008	0.008
53298	England	2016/17	B	B	275	ST-269 complex	Blood	0.047	0.008	0.004	0.003
53299	England	2016/17	B	B	32	ST-32 complex	Blood	0.064	0.008	0.004	0.004
53302	Wales	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.004
53303	England	2016/17	C	C	11	ST-11 complex	Blood	0.047	0.012	0.004	0.004
53304	England	2016/17	C	C	11	ST-11 complex	Blood	0.25	0.016	0.004	0.004
53305	Wales	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.016	0.004	0.002
53306	England	2016/17	C	C	11	ST-11 complex	Blood	0.064	0.047	0.008	0.004
53310	England	2016/17	B	B	1163	ST-269 complex	Blood	0.094	0.004	0.004	0.004
53311	England	2016/17	B	B	213	ST-213 complex	Blood	0.19	0.012	0.004	0.006
53312	England	2016/17	E	E	4146	ST-60 complex	Blood	0.047	0.032	0.008	0.004
53313	England	2016/17	B	B	9180	ST-269 complex	Blood	0.125	0.064	0.004	0.003
53314	England	2016/17	B	B	9180	ST-269 complex	Blood	0.19	0.032	0.008	0.004
53316	Wales	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.003
53317	England	2016/17	C	C	11	ST-11 complex	Blood	0.125	0.032	0.008	0.008
53318	England	2016/17	Y	Y	12176	ST-23 complex	Blood	0.047	0.004	0.004	0.003

53319	England	2016/17	B	B	213	ST-213 complex	Blood	0.25	0.016	0.004	0.008
53320	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.064	0.008	0.004	0.002
53321	England	2016/17	B	B	7460	ST-32 complex	Blood	0.25	0.004	0.004	0.004
53324	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.004
53326	England	2016/17	Y	Y	168	ST-167 complex	Blood	0.047	0.006	0.008	0.003
53327	Wales	2016/17	Y	Y	1627	ST-167 complex	Blood	0.064	0.006	0.004	0.004
53329	England	2016/17	B	B	213	ST-213 complex	Blood	0.047	0.008	0.004	0.003
53330	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.094	0.008	0.004	0.006
53331	England	2016/17	B	B	10269	ST-41/44 complex	Blood	0.125	0.008	0.004	0.003
53332	England	2016/17	B	B	575	ST-213 complex	Blood	0.125	0.008	0.004	0.003
53333	England	2016/17	B	B	1791	ST-269 complex	Blood	0.047	0.008	0.004	<0.002
53334	England	2016/17	Y	Y	1378	ST-23 complex	Blood	0.047	0.004	0.004	0.004
53335	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.125	0.004	0.004	0.004
53336	England	2016/17	B	B	749	ST-32 complex	Blood	0.125	0.003	0.004	0.004
53337	Wales	2016/17	B	B	12992	UA	Blood	0.064	0.006	0.004	0.004
53342	England	2016/17	B	B	1572	ST-1572 complex	Blood	0.125	0.004	0.004	0.004
53345	England	2016/17	B	B	213	ST-213 complex	Blood	0.047	0.008	0.004	0.003
53348	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.125	0.016	0.004	0.003
53349	England	2016/17	B	B	162	ST-162 complex	Blood	0.047	0.002	0.004	0.003
53351	England	2016/17	B	B	213	ST-213 complex	Blood	0.047	0.047	0.004	0.003
53353	England	2016/17	Y	Y	23	ST-23 complex	Blood	0.25	0.006	0.004	0.004
53356	Wales	2016/17	B	B	1096	ST-32 complex	Blood	0.047	0.032	0.004	0.004
53357	England	2016/17	B	B	3818	ST-41/44 complex	Blood	0.047	0.006	0.004	0.003
53359	England	2016/17	B	B	1161	ST-269 complex	Blood	0.047	0.008	0.004	0.003
53361	England	2016/17	B	B	11487	ST-41/44 complex	CSF	0.047	0.012	0.004	0.002
53362	Wales	2016/17	C	C	11	ST-11 complex	Blood	0.047	0.023	0.008	0.004
53363	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.047	0.008	0.004	0.002
53364	England	2016/17	B	B	1157	ST-1157 complex	Blood	0.032	0.004	0.004	0.002
53366	England	2016/17	B	B	12993	ST-213 complex	CSF	0.047	0.032	0.004	0.004
53370	England	2016/17	B	B	839	ST-41/44 complex	CSF	0.047	0.006	0.004	0.003
53373	England	2016/17	B	B	340	ST-41/44 complex	Blood	0.047	0.008	0.004	0.004
57961	England	2017/18	B	B	41	ST-41/44 complex	CSF	0.19	0.006	0.003	0.006
60546	England	2017/18	B	B	1354	ST-269 complex	Blood	0.047	0.008	0.004	0.002
60547	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.19	0.016	0.004	0.004
60548	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.004	0.004
60550	England	2017/18	NG	B	13702	UA	Blood	0.047	0.032	0.004	0.003
60551	England	2017/18	B	B	13703	ST-41/44 complex	Blood	0.19	0.006	0.004	0.004
60556	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
60560	Northern Ireland	2017/18	B	B	1163	ST-269 complex	Blood	0.25	0.006	0.004	0.006
60563	England	2016/17	B	B	1161	ST-269 complex	Blood	0.25	0.023	0.004	0.006
60564	Wales	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.008	0.003
60567	England	2017/18	C	C	11	ST-11 complex	Blood	0.094	0.012	0.006	0.004
60568	England	2017/18	C	C	11	ST-11 complex	Pericardium	0.25	0.023	0.004	0.008
60569	Northern Ireland	2017/18	Y	Y	23	ST-23 complex	Blood	0.047	0.004	0.003	0.002
60570	England	2016/17	B	B	457	ST-35 complex	Blood	0.047	0.047	0.008	0.004
60574	Wales	2017/18	B	B	13704	ST-461 complex	CSF	0.25	0.006	0.003	0.008
60577	England	2017/18	B	B	1195	ST-269 complex	Blood	0.032	0.012	0.004	<0.002
60580	England	2016/17	NG	NG	NK	INCOMPLETE MLST	Blood	0.023	0.032	0.004	0.002
60582	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.125	0.004	0.004	<0.002
60583	England	2017/18	B	B	13705	ST-41/44 complex	Blood	0.094	0.012	0.004	0.003
60585	England	2017/18	C	C	11	ST-11 complex	Blood	0.38	0.094	0.004	0.004
60586	England	2017/18	B	B	13706	ST-213 complex	Blood	0.047	0.016	0.004	0.003
60588	England	2016/17	C	C	11	ST-11 complex	Blood	0.38	0.094	0.004	0.008
60593	England	2016/17	B	B	13707	UA	Blood	0.125	0.008	0.006	0.006
60594	England	2016/17	B	B	269	ST-269 complex	Blood	0.032	0.016	0.004	<0.002
60595	England	2017/18	B	B	269	ST-269 complex	Blood	0.032	0.004	0.004	0.004
60596	England	2017/18	C	C	13708	UA	Blood	0.047	0.012	0.004	0.003
60598	England	2016/17	B	B	1161	ST-269 complex	Blood	0.064	0.016	0.008	0.004
60600	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.25	0.004	0.004	0.003
60602	Wales	2017/18	W	W	11	ST-11 complex	Blood	0.094	0.006	0.004	0.004
60604	England	2017/18	B	B	1194	ST-41/44 complex	Blood	0.064	0.006	0.004	0.003
60605	Wales	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.023	0.008	0.004
60608	England	2017/18	B	B	162	ST-162 complex	Blood	0.125	0.008	0.004	0.003
60609	England	2017/18	B	B	269	ST-269 complex	Blood	0.032	0.023	0.004	0.002
60610	England	2016/17	B	B	269	ST-269 complex	Blood	0.047	0.008	0.008	0.004
60615	England	2016/17	C	C	11	ST-11 complex	Pericardium	0.094	0.023	0.008	0.004
60617	England	2017/18	C	C	33	ST-32 complex	Blood	0.064	0.008	0.004	0.002
60618	England	2017/18	B	B	1161	ST-269 complex	Blood	0.064	0.047	0.004	0.003
60620	England	2016/17	B	B	275	ST-269 complex	Blood	0.125	0.032	0.008	0.006
60622	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.25	0.047	0.004	0.003
60623	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.125	0.004	0.004	0.006
60625	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.094	0.006	0.004	0.002
60626	England	2017/18	B	B	749	ST-32 complex	Blood	0.125	0.004	0.004	0.008
60627	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.25	0.023	0.004	0.004
60628	England	2016/17	W	W	114	ST-22 complex	Blood	0.064	0.016	0.004	0.003
60630	Wales	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.004	0.003
60633	England	2016/17	B	B	485	ST-41/44 complex	CSF	0.19	0.016	0.008	0.003
60635	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.016	0.008	0.006
60636	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.004
60637	England	2017/18	B	B	1341	ST-41/44 complex	Blood	0.25	0.012	0.004	0.004
60638	England	2016/17	B	B	13709	ST-41/44 complex	Blood	0.064	0.008	0.004	<0.002
60640	England	2017/18	B	B	7981	ST-269 complex	Blood	0.094	0.016	0.006	0.002
60641	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.19	0.012	0.006	0.004
60643	England	2016/17	B	B	1162	UA	Blood	0.032	0.032	0.004	0.003
60644	England	2017/18	B	B	461	ST-461 complex	Blood	0.25	0.023	0.004	0.008

60647	England	2017/18	B	B	1946	ST-461 complex	Blood	0.25	0.016	0.004	0.004
60648	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.003	0.004
60650	England	2016/17	C	C	11	ST-11 complex	Blood	0.25	0.032	0.004	0.125
60652	England	2017/18	Y	Y	11846	ST-103 complex	Blood	0.125	0.008	0.004	0.008
60653	England	2017/18	W	W	13710	UA	Blood	0.094	0.032	0.004	0.003
60654	England	2017/18	B	B	32	ST-32 complex	Blood	0.064	0.012	0.004	0.004
60655	England	2016/17	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.008	0.004	0.004
60658	England	2017/18	B	B	213	ST-213 complex	Blood	0.25	0.012	0.004	0.004
60659	England	2017/18	B	B	32	ST-32 complex	Blood	0.064	0.012	0.006	0.004
60660	England	2016/17	B	B	5151	UA	Blood	0.19	0.008	0.004	0.004
60662	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.008	0.004	0.004
60665	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.125	0.006	0.004	0.004
60666	England	2017/18	B	B	13711	UA	Blood	0.19	0.006	0.006	0.012
60668	England	2016/17	B	B	13712	UA	Blood	0.064	0.006	0.004	0.004
60670	England	2017/18	B	B	213	ST-213 complex	Blood	0.032	0.032	0.004	0.003
60673	England	2016/17	B	B	3754	ST-41/44 complex	Blood	0.19	0.023	0.004	0.004
60677	England	2017/18	B	B	2314	ST-41/44 complex	Blood	0.047	0.006	0.004	0.003
60678	England	2016/17	B	B	8597	UA	CSF	0.38	0.032	0.004	0.004
60679	England	2016/17	B	B	1157	ST-1157 complex	Blood	0.032	<0.002	0.002	0.003
60683	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.004
60684	England	2017/18	B	B	7152	ST-1572 complex	Blood	0.19	0.004	0.003	0.004
60687	England	2017/18	B	B	33	ST-32 complex	Blood	0.047	0.006	0.004	0.002
60688	Northern Ireland	2017/18	B	B	13713	ST-269 complex	Blood	0.047	0.032	0.003	0.003
60689	Wales	2017/18	W	W	11	ST-11 complex	Blood	0.19	0.047	0.006	0.012
60690	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.064	0.008	0.004	0.003
60693	England	2017/18	W	W	10033	UA	Blood	0.064	0.032	0.004	0.008
60695	England	2016/17	Y	Y	3582	ST-23 complex	Blood	0.047	0.012	0.008	0.003
60697	England	2017/18	B	B	275	ST-269 complex	Blood	0.064	0.006	0.004	0.003
60698	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.016	0.004	0.004
60702	England	2017/18	B	B	213	ST-213 complex	Blood	0.032	0.032	0.004	0.003
60703	England	2017/18	B	B	6607	ST-213 complex	Blood	0.19	0.006	0.004	0.003
60705	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.004	0.003
60711	England	2017/18	Y	Y	3582	ST-23 complex	Blood	0.094	0.008	0.004	0.008
60712	Wales	2017/18	B	B	1161	ST-269 complex	Blood	0.19	0.012	0.004	0.004
60713	England	2016/17	W	W	1286	ST-22 complex	Blood	0.094	0.016	0.004	0.004
60715	Northern Ireland	2017/18	Y	Y	1655	ST-23 complex	Blood	0.016	0.003	0.003	<0.002
60716	England	2017/18	B	B	9200	ST-41/44 complex	Blood	0.094	0.006	0.002	0.004
60721	England	2017/18	Y	Y	1466	ST-174 complex	Blood	0.094	0.008	0.003	0.006
60725	England	2016/17	B	B	839	ST-41/44 complex	Blood	0.023	0.016	0.004	0.002
60732	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.19	0.004	0.004	0.006
60733	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.032	0.032	0.004	0.002
60734	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.032	0.003	0.004	0.002
60735	England	2016/17	C	C	11	ST-11 complex	Blood	0.064	0.008	0.004	0.004
60737	England	2017/18	B	B	162	ST-162 complex	Blood	0.19	0.012	0.004	0.004
60738	England	2017/18	B	B	213	ST-213 complex	Blood	0.38	0.008	0.004	0.008
60739	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.032	0.003	0.003	0.002
60740	England	2016/17	B	B	7670	ST-41/44 complex	Blood	0.19	0.023	0.004	0.004
60743	England	2017/18	B	B	1214	ST-269 complex	Blood	0.032	0.012	0.004	0.008
60744	England	2017/18	B	B	11487	ST-41/44 complex	CSF	0.047	0.006	0.004	0.003
60747	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.008	0.004	0.004
60748	England	2016/17	B	B	213	ST-213 complex	Blood	0.38	0.047	0.004	0.008
60749	England	2017/18	B	B	136	ST-41/44 complex	Blood	0.25	0.016	0.003	0.006
60751	England	2016/17	B	B	4033	ST-41/44 complex	Blood	0.125	0.004	0.004	0.003
60752	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.008	0.003	0.003
60755	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.19	0.016	0.004	0.004
60757	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.032	0.008	0.008	0.004
60758	England	2017/18	B	B	3754	ST-41/44 complex	Blood	0.047	0.023	0.004	0.004
60761	Northern Ireland	2017/18	B	B	10550	ST-35 complex	Blood	0.38	0.008	0.004	0.012
60764	England	2017/18	C	C	11	ST-11 complex	Joint	0.064	0.023	0.006	0.004
60766	England	2016/17	B	B	162	ST-162 complex	Blood	0.19	0.012	0.004	0.006
60767	England	2017/18	B	B	13714	ST-41/44 complex	CSF	0.125	0.006	0.004	0.004
60768	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.064	0.008	0.004	0.003
60771	England	2017/18	B	B	33	ST-32 complex	Blood	0.047	0.032	0.004	0.004
60772	England	2016/17	B	B	13715	UA	Blood	0.064	0.003	0.004	0.004
60774	England	2017/18	B	B	4531	ST-213 complex	Blood	0.19	0.023	0.003	0.004
60775	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.003
60777	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.008	0.004	0.004
60779	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.25	0.012	0.004	0.004
60780	England	2017/18	W	W	12116	ST-22 complex	Blood	0.016	0.004	0.004	0.002
60781	England	2017/18	B	B	340	ST-41/44 complex	Blood	0.047	0.094	0.008	0.003
60782	England	2017/18	B	B	213	ST-213 complex	Blood	0.047	0.032	0.004	0.004
60783	England	2016/17	B	B	13716	ST-41/44 complex	Blood	0.125	0.003	0.004	0.004
60785	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
60787	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.19	0.012	0.004	0.004
60788	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.125	0.047	0.004	0.003
60789	England	2017/18	B	B	13717	UA	Blood	0.25	0.006	0.003	0.004
60793	England	2017/18	B	B	2314	ST-41/44 complex	Blood	0.064	0.004	0.004	0.003
60798	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.032	0.003	0.004	0.003
60799	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.004	0.004
60804	Wales	2016/17	B	B	3893	ST-41/44 complex	CSF	0.125	0.023	0.004	0.004
60807	England	2017/18	B	B	213	ST-213 complex	Blood	0.25	0.008	0.004	0.004
60809	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.003
60810	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
60811	England	2016/17	B	B	8750	ST-213 complex	Blood	0.19	0.032	0.004	0.008
60813	England	2017/18	B	B	213	ST-213 complex	CSF	0.064	0.016	0.004	0.003

60814	England	2017/18	B	B	13718	ST-162 complex	Blood	0.25	0.016	0.004	0.006
60815	England	2016/17	B	B	1161	ST-269 complex	Blood	0.19	0.008	0.004	0.003
60816	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.032	0.004	0.004
60817	England	2017/18	C	C	13719	UA	Blood	0.25	0.064	0.004	0.004
60818	England	2017/18	B	B	33	ST-32 complex	Blood	0.064	0.032	0.004	0.004
60819	Wales	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.004
60820	England	2017/18	B	B	18	ST-18 complex	Blood	0.047	0.016	0.004	0.006
60821	England	2017/18	W	W	2477	ST-60 complex	Blood	0.047	0.002	0.003	<0.002
60822	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.016	0.004	0.003
60823	England	2017/18	B	B	1159	UA	Blood	0.125	0.004	0.004	0.004
60824	England	2017/18	B	B	213	ST-213 complex	Blood	0.023	0.003	0.003	0.003
60828	Wales	2017/18	C	C	11	ST-11 complex	Blood	0.032	0.023	0.008	0.003
60829	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.004
60831	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.125	0.016	0.008	0.008
60834	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.003
60835	England	2016/17	B	B	213	ST-213 complex	Blood	0.032	0.032	0.004	0.006
60839	England	2017/18	B	B	8988	UA	Blood	0.25	0.012	0.006	0.006
60840	England	2017/18	NG	C	278	ST-35 complex	Blood	0.19	0.012	0.004	0.003
60843	England	2017/18	B	B	154	ST-41/44 complex	Blood	0.125	0.004	0.004	0.004
60845	England	2017/18	C	C	11	ST-11 complex	Blood	0.25	0.012	0.004	0.008
60846	England	2017/18	B	B	571	ST-41/44 complex	CSF	0.064	0.006	0.004	0.003
60852	England	2017/18	B	B	9193	ST-213 complex	Blood	0.047	0.032	0.004	0.003
60856	England	2017/18	B	B	1194	ST-41/44 complex	Blood	0.047	0.004	0.004	0.002
60858	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.003
60859	Wales	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.004	0.003
60861	England	2017/18	B	B	2477	ST-60 complex	Blood	0.125	0.023	0.004	0.006
60862	England	2016/17	B	B	1163	ST-269 complex	Blood	0.094	0.003	0.004	0.006
60865	England	2017/18	Y	Y	168	ST-167 complex	Blood	0.023	0.003	0.003	<0.002
60866	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.004	0.003
60871	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.002
60872	England	2016/17	C	C	11	ST-11 complex	Blood	0.047	0.016	0.004	0.006
60874	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.006
60875	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.047	0.008	0.004	0.003
60882	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.25	0.004	0.004	0.008
60885	England	2016/17	B	B	41	ST-41/44 complex	Blood	0.094	0.016	0.004	0.002
60887	England	2017/18	B	B	7193	ST-213 complex	Blood	0.19	0.012	0.008	0.008
60888	England	2017/18	B	B	1831	UA	Blood	0.064	0.032	0.004	0.004
60890	England	2016/17	B	B	5151	UA	Blood	0.094	0.094	0.004	0.006
60892	England	2017/18	NG	CNL	13722	ST-41/44 complex	Blood	0.023	0.006	0.004	0.002
60894	England	2017/18	B	B	213	ST-213 complex	Blood	0.25	0.012	0.004	0.003
60897	England	2017/18	B	B	13723	ST-461 complex	Blood	0.125	0.004	0.002	0.004
60899	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.023	0.004	0.003
60900	England	2016/17	B	B	1097	ST-41/44 complex	Blood	0.032	0.008	0.004	0.003
60901	England	2017/18	B	B	13724	ST-60 complex	Blood	0.25	0.006	0.004	0.008
60902	Northern Ireland	2016/17	Y	Y	11280	ST-23 complex	Blood	0.064	0.006	0.004	0.004
60909	England	2017/18	B	B	1161	ST-269 complex	Blood	0.125	0.006	0.008	0.004
60910	England	2017/18	B	B	13725	ST-865 complex	Blood	0.047	0.006	0.003	0.002
60911	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.003	0.002
60912	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.004	0.004
60914	England	2017/18	C	C	11	ST-11 complex	Blood	0.125	0.016	0.008	0.008
60915	England	2017/18	B	B	1163	ST-269 complex	Blood	0.125	0.004	0.004	0.003
60916	England	2017/18	Y	Y	23	ST-23 complex	Blood	0.094	<0.002	0.003	0.004
60917	England	2016/17	B	B	213	ST-213 complex	Blood	0.047	0.023	0.004	0.004
60920	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.012	0.004	0.004
60924	England	2017/18	B	B	NK	INCOMPLETE MLST	Blood	0.064	0.064	0.004	0.003
60930	England	2016/17	B	B	1097	ST-41/44 complex	Blood	0.064	0.016	0.004	0.003
60932	Wales	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.016	0.004	0.003
60933	England	2017/18	B	B	9199	UA	Blood	0.125	0.004	0.003	0.004
60935	England	2016/17	B	B	NK	INCOMPLETE MLST	Blood	0.19	0.006	0.004	0.003
60937	England	2017/18	C	C	11	ST-11 complex	Blood	0.125	0.008	0.008	0.004
60938	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.19	0.006	0.004	0.004
60940	England	2016/17	B	B	485	ST-41/44 complex	Blood	0.094	0.008	0.004	0.008
60942	England	2016/17	B	B	46	ST-41/44 complex	Blood	0.047	0.008	0.004	0.003
60945	England	2017/18	B	B	1194	ST-41/44 complex	Blood	0.047	0.006	0.004	0.002
60946	England	2017/18	NG	B	1163	ST-269 complex	Blood	0.19	0.004	0.002	<0.002
60950	England	2017/18	B	B	13726	ST-269 complex	Blood	0.047	0.006	0.004	0.002
60951	England	2017/18	W	W	3651	ST-22 complex	Blood	0.064	0.008	0.004	0.004
60952	England	2016/17	C	C	11	ST-11 complex	Blood	0.064	0.012	0.004	0.006
60955	England	2017/18	B	B	269	ST-269 complex	CSF	0.016	0.003	0.004	0.002
60959	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.012	0.004	0.004
60960	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.003
60962	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.008	0.004	0.004
60964	England	2017/18	Y	Y	23	ST-23 complex	Blood	0.38	0.008	0.003	0.012
60968	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.032	0.003	0.003	0.002
60969	England	2017/18	Y	Y	12176	ST-23 complex	Blood	0.064	0.008	0.004	0.003
60970	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.004
60972	England	2017/18	B	B	275	ST-269 complex	Blood	0.047	0.094	0.006	0.004
60973	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.047	0.012	0.004	0.003
60974	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.008	0.006	0.004
60975	England	2016/17	B	B	1159	UA	Blood	0.047	0.004	0.004	0.004
60977	England	2017/18	Y	Y	11280	ST-23 complex	Blood	0.064	0.006	0.004	0.006
60978	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
60979	England	2017/18	B	B	13727	ST-41/44 complex	Blood	0.25	0.006	0.004	0.004
60980	England	2016/17	B	B	2362	ST-41/44 complex	Blood	0.19	0.008	0.008	0.006
60981	England	2017/18	Y	Y	1657	ST-23 complex	Blood	0.064	0.004	0.004	0.003

60982	England	2016/17	B	B	213	ST-213 complex	Blood	0.064	0.016	0.004	0.006
60983	Northern Ireland	2016/17	C	C	11	ST-11 complex	Blood	0.047	0.023	0.004	0.002
60985	England	2017/18	Y	Y	23	ST-23 complex	Blood	0.064	0.004	0.004	0.004
60986	England	2017/18	Y	Y	3582	ST-23 complex	Blood	0.094	0.047	0.003	0.006
60988	England	2016/17	W	W	2977	ST-174 complex	Blood	0.125	0.016	0.004	0.008
60989	Wales	2017/18	B	B	41	ST-41/44 complex	Blood	0.125	0.003	0.004	0.012
60991	England	2017/18	B	B	2314	ST-41/44 complex	Blood	0.047	0.006	0.003	0.003
60992	Wales	2016/17	Y	Y	23	ST-23 complex	Blood	0.064	0.008	0.004	0.006
60993	England	2016/17	B	B	269	ST-269 complex	Blood	0.047	0.008	0.008	0.002
60995	England	2017/18	B	B	13728	ST-269 complex	Blood	0.25	0.008	0.004	0.006
60996	England	2017/18	B	B	2314	ST-41/44 complex	Blood	0.125	0.023	0.004	0.003
60999	England	2017/18	B	B	749	ST-32 complex	Blood	0.19	0.004	0.006	0.006
61001	England	2017/18	B	B	1195	ST-269 complex	Blood	0.094	0.008	0.004	0.004
61005	England	2016/17	B	B	43	ST-41/44 complex	Joint	0.064	0.012	0.004	0.004
61006	England	2017/18	C	C	11	ST-11 complex	Blood	0.047	0.016	0.004	0.003
61007	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
61009	England	2017/18	B	B	2203	ST-41/44 complex	Blood	0.064	0.012	0.004	0.003
61010	England	2016/17	B	B	275	ST-269 complex	Blood	0.023	0.008	0.004	<0.002
61012	Wales	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.012	0.006	0.003
61013	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.094	0.016	0.004	0.008
61014	England	2017/18	B	B	13730	ST-41/44 complex	Blood	0.047	0.006	0.003	0.003
61015	England	2016/17	Y	Y	1655	ST-23 complex	Blood	0.064	0.016	0.004	0.004
61016	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.004
61017	England	2017/18	B	B	43	ST-41/44 complex	Blood	0.064	0.006	0.004	0.002
61018	England	2017/18	B	B	9989	ST-32 complex	Blood	0.19	0.016	0.004	0.006
61019	England	2017/18	B	B	2380	ST-35 complex	Blood	0.047	0.008	0.004	0.003
61021	England	2017/18	NG	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.003
61023	England	2017/18	C	C	13731	ST-11 complex	Blood	0.047	0.032	0.004	0.004
61024	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.19	0.008	0.006	0.003
61025	Wales	2017/18	B	B	7460	ST-32 complex	Blood	0.25	0.012	0.004	0.006
61026	England	2017/18	B	B	749	ST-32 complex	Blood	0.19	0.004	0.004	0.006
61027	England	2016/17	B	B	154	ST-41/44 complex	Blood	0.064	0.008	0.008	0.003
61028	England	2016/17	B	B	213	ST-213 complex	Blood	0.094	0.004	0.004	0.002
61029	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.064	0.008	0.004	0.002
61030	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.004
61032	England	2016/17	C	C	11	ST-11 complex	Blood	0.094	0.016	0.008	0.008
61034	England	2017/18	B	B	34	ST-32 complex	Blood	0.19	0.012	0.004	0.004
61036	Wales	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.003
61039	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.094	0.004	0.004	0.004
61040	England	2017/18	B	B	213	ST-213 complex	Blood	0.064	0.023	0.004	0.003
61983	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.016	0.004	0.004
61984	England	2018/19	C	C	11	ST-11 complex	Blood	0.064	0.016	0.006	0.003
61985	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.008	0.004	0.004
61986	England	2017/18	C	C	13919	ST-11 complex	Blood	0.047	0.008	0.004	0.004
61987	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.012	0.006	0.006
61988	England	2018/19	C	C	NK	INCOMPLETE MLST	Blood	0.047	0.023	0.003	0.004
61989	England	2018/19	C	C	11	ST-11 complex	Blood	0.047	0.023	0.008	0.003
61990	England	2018/19	C	C	11	ST-11 complex	Blood	0.094	0.023	0.006	0.004
63435	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.19	0.008	0.004	0.006
63436	England	2018/19	B	B	2314	ST-41/44 complex	Blood	0.19	0.004	0.004	0.003
63439	England	2017/18	B	B	9775	ST-32 complex	Blood	0.19	0.064	0.003	0.004
63440	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.125	0.003	0.004	0.002
63442	England	2018/19	B	B	213	ST-213 complex	Blood	0.25	0.012	0.003	0.006
63445	England	2017/18	B	B	35	ST-35 complex	Blood	0.19	0.047	0.004	0.004
63446	England	2017/18	B	B	4124	ST-269 complex	Blood	0.125	0.003	0.003	0.004
63447	England	2018/19	B	B	13441	ST-213 complex	Blood	0.047	0.016	0.003	0.002
63451	England	2017/18	B	B	15562	ST-213 complex	Blood	0.047	0.012	0.004	0.003
63452	England	2017/18	B	B	34	ST-32 complex	Blood	0.19	0.047	0.004	0.004
63454	England	2017/18	B	B	15560	ST-213 complex	Blood	0.032	0.004	0.004	0.002
63455	England	2017/18	B	B	1194	ST-41/44 complex	Blood	0.047	0.016	0.004	0.003
63456	England	2017/18	B	B	3635	ST-213 complex	Blood Culture	0.064	0.016	0.003	0.003
63457	England	2018/19	B	B	269	ST-269 complex	Blood	0.047	0.004	0.004	<0.002
63458	England	2018/19	B	B	NK	INCOMPLETE MLST	Blood	0.047	0.006	0.004	0.002
63459	England	2018/19	B	B	15563	ST-461 complex	Blood	0.032	0.006	0.003	0.002
63460	England	2018/19	B	B	41	ST-41/44 complex	Blood	0.047	0.012	0.008	<0.002
63461	England	2018/19	B	B	1194	ST-41/44 complex	Blood	0.064	0.006	0.004	0.002
63468	England	2017/18	B	B	213	ST-213 complex	Blood	0.047	0.047	0.004	0.003
63469	England	2017/18	B	B	1161	ST-269 complex	Blood	0.19	0.006	0.002	0.003
63470	England	2018/19	B	B	15531	ST-18 complex	CSF	0.047	0.003	0.004	0.004
63473	England	2017/18	B	B	8068	ST-282 complex	Blood	0.047	0.016	0.003	0.002
63474	England	2018/19	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.004	0.002
63475	England	2018/19	B	B	41	ST-41/44 complex	Blood	0.047	0.006	0.004	0.003
63476	England	2018/19	B	B	9193	ST-213 complex	Blood	0.047	0.016	0.004	0.002
63477	England	2018/19	B	B	15542	ST-60 complex	Blood	0.094	0.006	0.002	<0.002
63478	England	2018/19	B	B	2314	ST-41/44 complex	Blood	0.125	0.008	0.003	0.004
63479	England	2018/19	B	B	1475	ST-41/44 complex	Blood	0.064	0.012	0.004	0.003
63480	England	2018/19	B	B	32	ST-32 complex	Blood	0.047	0.094	0.008	0.002
63484	England	2017/18	B	B	9180	ST-269 complex	Blood	0.19	0.008	0.006	0.004
63485	England	2017/18	B	B	1161	ST-269 complex	Blood	0.094	0.047	0.004	0.004
63486	England	2017/18	B	B	839	ST-41/44 complex	Blood Culture	0.064	0.008	0.004	0.003
63487	England	2018/19	B	B	1194	ST-41/44 complex	Blood	0.047	0.003	0.004	<0.002
63488	England	2018/19	B	B	213	ST-213 complex	Blood	0.047	0.008	0.004	0.003
63491	England	2017/18	B	B	2314	ST-41/44 complex	Blood	0.094	0.012	0.003	0.002
63492	England	2018/19	B	B	749	ST-32 complex	Blood	0.125	0.006	0.002	0.006
63493	England	2018/19	B	B	213	ST-213 complex	Blood	0.047	0.008	0.004	0.003

63494	England	2018/19	B	B	18	ST-18 complex	Blood	0.25	0.012	0.003	0.008
63496	England	2018/19	B	B	5682	ST-32 complex	Blood	0.25	0.008	0.004	0.004
63497	England	2018/19	B	B	213	ST-213 complex	CSF	0.5	0.023	0.008	0.006
63498	England	2018/19	B	B	46	ST-41/44 complex	Blood	0.023	0.023	0.004	<0.002
63499	England	2018/19	B	B	1157	ST-1157 complex	Blood	0.125	0.004	0.004	0.003
63500	England	2018/19	B	B	11306	UA	Blood	0.064	0.047	0.006	0.002
63501	England	2018/19	B	B	5682	ST-32 complex	Blood	0.25	0.012	0.008	0.004
63503	England	2018/19	B	B	41	ST-41/44 complex	Blood	0.094	0.023	0.006	0.003
63504	England	2018/19	B	B	1159	UA	Blood Culture	0.25	0.006	0.004	0.004
63505	England	2018/19	B	B	3478	ST-41/44 complex	Blood	0.19	0.047	0.004	0.006
63506	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.38	0.006	0.006	0.006
63507	England	2018/19	B	B	15533	UA	Blood	0.125	0.032	0.004	0.004
63508	England	2018/19	B	B	213	ST-213 complex	Blood	0.064	0.064	0.008	0.002
63509	England	2018/19	B	B	1194	ST-41/44 complex	Blood	0.064	0.006	0.006	<0.002
63510	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.38	0.064	0.008	0.004
63511	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.094	0.008	0.006	0.002
63512	England	2018/19	B	B	162	ST-162 complex	Blood	0.25	0.016	0.008	0.003
63513	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.094	0.008	0.008	0.004
63515	England	2018/19	B	B	11539	UA	Blood	0.25	0.016	0.003	0.016
63516	England	2018/19	B	B	14129	UA	Blood	0.094	0.016	0.006	0.003
63517	England	2018/19	B	B	7460	ST-32 complex	Blood	0.25	0.125	0.004	0.006
63518	England	2018/19	B	B	32	ST-32 complex	Blood	0.047	0.006	0.004	0.003
63519	England	2018/19	B	B	33	ST-32 complex	Blood	0.047	0.006	0.004	0.002
63520	England	2018/19	B	B	2288	ST-41/44 complex	Blood	0.047	0.032	0.006	0.003
63521	England	2018/19	B	B	7460	ST-32 complex	Blood	0.38	0.008	0.004	0.006
63522	England	2018/19	B	B	6765	ST-213 complex	Blood	0.094	0.016	0.008	0.003
63523	England	2018/19	B	B	15526	ST-41/44 complex	Blood	0.38	0.094	0.006	0.004
63526	England	2018/19	B	B	1774	ST-269 complex	Blood	0.047	0.016	0.004	0.002
63527	England	2018/19	B	B	40	ST-41/44 complex	Blood	0.047	0.006	0.006	0.002
63528	England	2018/19	B	B	15561	ST-269 complex	Blood	0.064	0.006	0.004	0.002
63529	England	2018/19	B	B	15534	UA	Blood	0.064	0.012	0.004	0.002
63530	England	2018/19	B	B	461	ST-461 complex	Blood	0.25	0.016	0.008	0.006
63531	England	2018/19	B	B	11755	ST-269 complex	Blood	0.125	0.094	0.004	0.003
63532	England	2018/19	B	B	1946	ST-461 complex	Blood	0.5	0.064	0.008	0.008
63533	England	2018/19	B	B	33	ST-32 complex	Blood	0.064	0.094	0.006	0.003
63535	England	2018/19	C	C	485	ST-41/44 complex	Blood	0.125	0.006	0.004	0.003
63536	England	2018/19	C	C	11	ST-11 complex	Blood	0.19	0.012	0.003	0.006
63539	England	2018/19	C	C	11	ST-11 complex	Blood	0.064	0.004	0.004	0.003
63540	England	2017/18	C	C	11	ST-11 complex	Blood	0.047	0.023	0.004	0.003
63542	England	2017/18	C	C	11	ST-11 complex	Blood	0.19	0.016	0.004	0.006
63543	England	2018/19	C	C	11	ST-11 complex	Blood	0.064	0.008	0.006	0.004
63544	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.023	0.004	0.003
63545	England	2018/19	C	C	5133	ST-103 complex	Blood	0.016	0.006	0.004	<0.002
63546	England	2018/19	C	C	11	ST-11 complex	Blood	0.064	0.006	0.004	0.003
63547	England	2018/19	C	C	11	ST-11 complex	Blood	0.064	0.032	0.004	0.003
63548	England	2018/19	C	C	11	ST-11 complex	Blood	0.064	0.012	0.004	0.004
63549	England	2018/19	C	C	11	ST-11 complex	Blood	0.094	0.012	0.006	0.004
63551	England	2018/19	C	C	11	ST-11 complex	Joint	0.38	0.094	0.006	0.023
63552	England	2018/19	C	C	5133	ST-103 complex	Blood	0.016	0.004	0.006	<0.002
63554	England	2018/19	C	C	11	ST-11 complex	Blood	0.064	0.016	0.006	0.003
63555	England	2018/19	C	C	11	ST-11 complex	Blood Culture	0.047	0.016	0.008	0.003
63557	England	2018/19	C	C	11	ST-11 complex	Blood	0.094	0.032	0.008	0.004
63558	England	2018/19	C	C	485	ST-41/44 complex	Blood	0.25	0.012	0.004	0.004
63559	England	2018/19	NG	B	14117	UA	Blood	0.125	0.023	0.06	0.004
63576	England	2017/18	W	W	9316	UA	Blood	0.125	0.023	0.006	<0.002
63613	England	2018/19	W	NK	3698	UA	Blood	0.125	0.016	0.006	0.006
63635	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.004
63636	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.003	0.004
63638	England	2017/18	Y	Y	23	ST-23 complex	Blood	0.064	0.004	0.004	0.003
63639	England	2017/18	Y	Y	15538	UA	Blood	0.38	0.012	0.004	0.008
63640	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.003
63641	England	2018/19	Y	Y	1655	ST-23 complex	Blood Culture	0.047	0.006	0.003	0.002
63642	England	2017/18	Y	Y	1655	ST-23 complex	CSF	0.047	0.003	0.003	0.004
63643	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.003	0.002
63645	England	2018/19	Y	Y	1466	ST-174 complex	Blood	0.125	0.064	0.002	0.004
63646	England	2017/18	Y	Y	23	ST-23 complex	Blood	0.047	0.003	0.006	0.004
63647	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.004	0.003
63648	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.004	0.003
63649	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.004	0.004
63650	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.032	0.006	0.004	0.002
63651	England	2017/18	Y	NK	15559	ST-23 complex	Blood	0.047	0.006	0.002	0.002
63653	England	2018/19	Y	Y	23	ST-23 complex	Blood	0.064	0.004	0.004	0.004
63654	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.004	0.002
63655	England	2017/18	Y	Y	1655	ST-23 complex	Joint	0.094	0.016	0.004	0.008
63656	England	2017/18	Y	NK	23	ST-23 complex	Blood	0.094	0.004	0.004	0.003
63657	England	2017/18	Y	Y	23	ST-23 complex	Blood	0.064	0.006	0.003	0.003
63659	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.002
63660	England	2018/19	Y	NK	1655	ST-23 complex	Blood	0.064	0.002	0.004	0.003
63661	England	2018/19	Y	NK	114	ST-22 complex	Blood	0.38	0.023	0.006	0.008
63662	England	2018/19	Y	Y	3582	ST-23 complex	Blood	0.125	0.008	0.004	0.006
63663	England	2018/19	Y	Y	23	ST-23 complex	Blood	0.064	0.008	0.004	0.004
63664	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.094	0.002	0.004	0.003
63666	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.003
63667	England	2018/19	Y	NK	3582	ST-23 complex	Blood	0.125	0.047	0.004	0.004
63668	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.064	0.008	0.004	0.003

63670	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.047	0.012	0.004	0.003
70987	England	2017/18	B	B	275	ST-269 complex	Blood	0.38	0.004	0.004	0.004
70988	England	2017/18	B	B	5151	UA	Blood	0.19	0.008	0.004	0.006
70989	England	2017/18	B	B	639	ST-32 complex	Blood	0.094	0.016	0.004	0.004
70991	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.003
70992	Northern Ireland	2017/18	B	B	269	ST-269 complex	Blood Culture	0.064	0.016	0.004	0.003
70993	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.064	0.006	0.004	0.002
70994	England	2017/18	B	B	12345	ST-32 complex	Blood	0.25	0.008	0.004	0.004
70999	England	2017/18	B	B	3117	ST-213 complex	Blood Culture	0.19	0.012	0.003	0.004
71001	Wales	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.004
71004	England	2017/18	B	B	8988	UA	Blood	0.19	0.016	0.004	0.004
71005	England	2017/18	B	B	275	ST-269 complex	Blood	0.094	0.012	0.004	0.003
71007	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.064	0.016	0.003	0.002
71008	Northern Ireland	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.016	0.006	0.006
71010	England	2017/18	B	B	136	ST-41/44 complex	Blood	0.064	0.002	0.002	0.002
71011	Wales	2017/18	C	C	5238	UA	Blood	0.125	0.008	0.004	0.004
71013	England	2017/18	Y	Y	23	ST-23 complex	Blood	0.064	0.004	0.004	0.006
71014	England	2017/18	B	B	7460	ST-32 complex	Blood	0.38	0.006	0.003	0.008
71015	England	2017/18	B	B	1194	ST-41/44 complex	Blood Culture	0.047	0.032	0.004	0.002
71016	England	2017/18	B	B	213	ST-213 complex	Blood	0.19	0.006	0.004	0.003
71017	England	2017/18	NG	C	467	ST-269 complex	CSF	0.125	0.004	0.004	0.004
71018	Northern Ireland	2017/18	B	B	1161	ST-269 complex	Blood	0.064	0.003	0.003	<0.002
71019	Wales	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.047	0.004	0.002
71020	England	2017/18	B	B	1721	ST-213 complex	Blood	0.064	0.012	0.004	0.004
71021	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.094	0.004	0.004	0.004
71022	England	2017/18	C	C	278	ST-35 complex	Blood	0.125	0.002	0.004	0.003
71023	England	2017/18	Y	Y	12176	ST-23 complex	Blood	0.064	0.012	0.004	0.006
71024	England	2017/18	B	B	1161	ST-269 complex	Blood Culture	0.094	0.008	0.004	0.003
71025	England	2017/18	B	B	1161	ST-269 complex	Blood Culture	0.094	0.012	0.004	0.004
71026	England	2017/18	Y	Y	3582	ST-23 complex	Blood Culture	0.125	0.016	0.004	0.006
71027	England	2017/18	B	B	4224	ST-213 complex	Blood	0.064	0.016	0.004	0.004
71028	England	2017/18	B	B	269	ST-269 complex	Blood	0.047	0.006	0.006	0.003
71029	England	2017/18	C	C	11	ST-11 complex	Blood	0.25	0.012	0.006	0.006
71034	England	2017/18	X	X	5063	UA	Blood	0.25	0.125	0.004	0.004
71035	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.004
71036	Wales	2017/18	C	C	11	ST-11 complex	Blood	0.047	0.023	0.004	0.003
71038	England	2017/18	C	C	11	ST-11 complex	Blood	0.19	0.094	0.003	0.008
71039	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.25	0.006	0.004	0.004
71040	England	2017/18	B	B	9989	ST-32 complex	Blood	0.19	0.008	0.003	0.006
71041	England	2017/18	B	B	1194	ST-41/44 complex	Blood	0.047	0.004	0.004	0.002
71042	England	2017/18	B	B	34	ST-32 complex	Blood Culture	0.19	0.016	0.003	0.008
71044	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.19	0.047	0.004	0.004
71047	Northern Ireland	2017/18	C	C	11	ST-11 complex	Blood	0.047	0.006	0.004	0.006
71048	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.094	0.004	0.006
71049	England	2017/18	C	C	11	ST-11 complex	Blood	0.023	0.002	0.003	0.002
71050	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.125	0.008	0.002	0.004
71053	England	2018/19	B	B	1161	ST-269 complex	Blood	0.064	0.006	0.004	0.004
71055	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.125	0.004	0.006	0.004
71056	England	2018/19	B	B	213	ST-213 complex	Blood	0.047	0.008	0.004	0.003
71057	Northern Ireland	2018/19	B	B	1161	ST-269 complex	Blood	0.19	0.008	0.006	0.004
71058	England	2018/19	B	B	2899	ST-213 complex	Blood	0.094	0.016	0.006	0.006
71059	England	2018/19	B	B	15212	ST-269 complex	Blood	0.032	0.032	0.004	0.002
71060	England	2018/19	C	C	11	ST-11 complex	Blood	0.047	0.047	0.008	0.003
71063	England	2018/19	B	B	1214	ST-269 complex	Blood	0.047	0.008	0.006	0.002
71065	England	2018/19	Y	Y	23	ST-23 complex	Blood	0.047	0.008	0.004	0.004
71066	England	2018/19	W	W	9316	UA	Blood Culture	0.125	0.008	0.004	0.003
71067	England	2018/19	B	B	3496	ST-213 complex	Blood	0.125	0.006	0.004	0.002
71068	England	2018/19	B	B	3737	ST-1157 complex	Blood	0.125	0.008	0.004	0.003
71070	England	2018/19	B	B	41	ST-41/44 complex	Blood	0.19	0.012	0.006	0.004
71072	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.094	0.006	0.006	0.006
71073	England	2018/19	B	B	7460	ST-32 complex	Blood	0.38	0.012	0.006	0.003
71074	England	2018/19	B	B	1097	ST-41/44 complex	Blood	0.047	0.006	0.003	0.003
71076	England	2018/19	B	B	41	ST-41/44 complex	Blood	0.19	0.016	0.006	0.004
71077	England	2018/19	C	C	11	ST-11 complex	Blood	0.125	0.016	0.006	0.004
71078	England	2018/19	B	B	41	ST-41/44 complex	Blood	0.064	0.047	0.004	0.002
71079	England	2018/19	B	B	15119	UA	Blood	0.047	0.012	0.008	0.002
71081	Wales	2018/19	B	B	485	ST-41/44 complex	CSF	0.25	0.023	0.008	0.003
71082	England	2018/19	B	B	12345	ST-32 complex	Blood	0.25	0.006	0.006	0.004
71083	England	2017/18	B	B	12173	ST-41/44 complex	Blood	0.19	0.008	0.004	0.004
71084	England	2017/18	B	B	6607	ST-213 complex	Blood	0.19	0.008	0.004	0.004
71085	England	2017/18	C	C	11	ST-11 complex	Blood	0.25	0.016	0.004	0.006
71086	Wales	2017/18	B	B	15205	ST-213 complex	Blood	0.064	0.012	0.004	0.003
71087	Wales	2017/18	B	B	1946	ST-461 complex	Blood	0.25	0.023	0.003	0.006
71090	England	2018/19	Y	Y	15206	ST-23 complex	Blood	0.094	0.004	0.004	0.003
71091	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.19	0.003	0.004	0.002
71092	England	2018/19	B	B	1976	UA	Blood	0.047	0.016	0.006	0.004
71093	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.094	0.006	0.006	0.006
71094	Wales	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.004	0.006	0.002
71095	England	2018/19	C	C	11	ST-11 complex	Blood	0.094	0.004	0.008	0.006
71096	England	2018/19	C	C	11	ST-11 complex	Blood	0.064	0.012	0.006	0.004
71097	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.006	0.003
71098	England	2018/19	B	B	749	ST-32 complex	Blood	0.19	0.023	0.008	0.006
71100	England	2018/19	B	B	15213	ST-41/44 complex	Blood	0.064	0.008	0.004	0.004
71101	England	2018/19	Y	Y	23	ST-23 complex	Blood	0.25	0.006	0.004	0.004
71103	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.19	0.004	0.004	0.002

71104	England	2018/19	B	B	213	ST-213 complex	CSF	0.19	0.006	0.004	0.006
71105	England	2018/19	B	B	275	ST-269 complex	CSF	0.25	0.006	0.006	0.003
71108	England	2018/19	NG	CNL	1103	ST-41/44 complex	Blood	0.125	0.032	0.004	0.002
71109	England	2018/19	B	B	213	ST-213 complex	Blood	0.064	0.047	0.004	0.003
71110	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.047	0.006	0.004	0.003
71111	England	2018/19	B	B	41	ST-41/44 complex	Blood	0.125	0.004	0.006	0.004
71112	England	2018/19	NG	B	213	ST-213 complex	Blood	0.25	0.012	0.006	0.008
71114	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.002	0.002
71116	England	2018/19	NG	X	5063	UA	Blood	0.25	0.023	0.006	0.012
71117	England	2018/19	W	W	8172	ST-865 complex	Blood	0.25	0.006	0.004	0.004
71118	England	2018/19	B	B	9293	ST-162 complex	Blood Culture	0.125	0.016	0.004	0.004
71119	England	2018/19	B	B	33	ST-32 complex	Blood	0.25	0.004	0.006	0.004
71120	England	2018/19	B	B	154	ST-41/44 complex	Blood	0.125	0.004	0.004	0.003
71122	England	2018/19	B	B	41	ST-41/44 complex	Blood	0.25	0.006	0.003	0.006
71123	England	2018/19	B	B	9193	ST-213 complex	Blood	0.094	0.004	0.004	0.008
71125	Wales	2018/19	C	C	11	ST-11 complex	Blood	0.064	0.004	0.006	0.003
71127	England	2018/19	B	B	162	ST-162 complex	Blood	0.064	0.006	0.004	0.003
71128	England	2018/19	C	C	11	ST-11 complex	Blood	0.38	0.032	0.004	0.008
71129	England	2018/19	B	B	1161	ST-269 complex	Blood	0.25	0.008	0.004	0.004
71130	England	2018/19	NG	B	865	ST-865 complex	Blood	0.064	0.016	0.002	0.006
71131	England	2018/19	C	C	15207	ST-11 complex	Blood	0.125	0.016	0.004	0.006
71132	Northern Ireland	2018/19	B	B	2314	ST-41/44 complex	Blood	0.125	0.032	0.003	0.004
71133	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.19	0.004	0.004	0.004
71134	England	2018/19	Y	Y	1657	ST-23 complex	Blood	0.094	0.003	0.004	0.004
71138	England	2018/19	B	B	213	ST-213 complex	Blood	0.125	0.004	0.003	0.004
71139	England	2018/19	B	B	213	ST-213 complex	Blood	0.064	0.012	0.004	0.004
71140	England	2018/19	B	B	1161	ST-269 complex	Blood	0.094	0.004	0.004	0.004
71141	England	2018/19	B	B	6349	ST-41/44 complex	Blood	0.25	0.064	0.004	0.008
71143	England	2018/19	B	B	749	ST-32 complex	Blood	0.38	0.008	0.006	0.012
71144	Wales	2018/19	Y	Y	1655	ST-23 complex	Blood	0.125	0.004	0.003	0.003
71146	England	2018/19	C	C	12227	ST-11 complex	Blood	0.064	0.008	0.004	0.004
71147	England	2018/19	B	B	482	ST-41/44 complex	Blood	0.125	0.032	0.006	0.004
71149	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.004	0.004
71150	England	2018/19	W	W	3859	ST-22 complex	Blood	0.125	0.008	0.004	0.003
71154	England	2018/19	B	B	275	ST-269 complex	Blood	0.047	0.006	0.006	0.004
71155	England	2018/19	B	B	11	ST-11 complex	Blood	0.19	0.012	0.004	0.008
71156	England	2018/19	Y	Y	23	ST-23 complex	Blood	0.047	0.002	0.003	0.003
71157	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.064	0.003	0.004	0.003
71158	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.25	0.003	0.004	0.006
71161	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.006	0.003
71163	England	2018/19	B	B	7670	ST-41/44 complex	Blood	0.19	0.002	0.004	0.004
71164	Wales	2018/19	B	B	15208	ST-269 complex	Blood	0.047	0.004	0.006	0.002
71165	England	2018/19	B	B	414	ST-41/44 complex	Blood	0.125	0.003	0.006	0.006
71166	England	2018/19	C	C	11	ST-11 complex	Blood	0.094	0.016	0.008	0.006
71167	England	2018/19	B	B	162	ST-162 complex	Blood	0.19	0.016	0.006	0.004
71168	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.003
71169	England	2018/19	B	B	2314	ST-41/44 complex	Blood	0.19	0.004	0.004	0.004
71171	England	2018/19	B	B	11221	ST-213 complex	Blood	0.19	0.016	0.004	0.004
71172	England	2018/19	B	B	23	ST-23 complex	Blood	0.094	0.004	0.004	0.006
71173	England	2018/19	B	B	1946	ST-461 complex	Blood	0.5	0.016	0.004	0.006
71174	England	2018/19	B	B	35	ST-35 complex	Blood	0.38	0.004	0.004	0.016
71175	England	2018/19	B	B	14117	UA	Blood	0.125	0.016	0.004	0.003
71176	England	2018/19	B	B	14117	UA	Blood	0.125	0.032	0.006	0.004
71177	England	2018/19	B	B	41	ST-41/44 complex	Blood	0.19	0.016	0.004	0.002
71178	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.19	0.032	0.004	0.003
85528	Northern Ireland	2017/18	B	B	4051	UA	Blood	0.064	0.032	0.003	0.003
85530	England	2017/18	C	C	485	ST-41/44 complex	Blood	0.19	0.008	0.004	0.004
85531	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.064	0.008	0.004	0.002
85533	Northern Ireland	2017/18	C	C	11	ST-11 complex	CSF	0.094	0.016	0.006	0.006
85536	England	2017/18	W	W	184	ST-22 complex	Blood	0.023	0.002	0.004	0.002
85537	England	2017/18	B	B	275	ST-269 complex	CSF	0.094	0.006	0.004	0.003
85539	Wales	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.004	0.006	0.003
85541	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.25	0.012	0.004	0.004
85542	England	2017/18	B	B	340	ST-41/44 complex	Blood	0.047	0.006	0.004	0.003
85544	England	2017/18	Y	Y	14356	ST-23 complex	Blood	0.064	0.004	0.004	0.003
85545	Wales	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.023	0.004	0.003
85547	England	2017/18	C	C	11	ST-11 complex	CSF	0.094	0.008	0.006	0.008
85548	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	<0.002	0.003
85549	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.125	0.008	0.004	0.004
85550	England	2017/18	B	B	162	ST-162 complex	Blood	0.047	0.008	0.004	0.003
85551	England	2017/18	B	B	2738	ST-269 complex	Blood	0.064	0.012	0.004	0.008
85553	England	2017/18	NG	B	485	ST-41/44 complex	CSF	0.19	0.008	0.004	0.006
85554	England	2017/18	B	B	14357	UA	Blood	0.064	0.012	0.004	0.002
85555	England	2017/18	B	B	14358	ST-269 complex	Blood	0.047	0.023	0.03	0.002
85558	England	2017/18	B	B	9193	ST-213 complex	Blood	0.064	0.032	0.006	0.004
85559	England	2017/18	B	B	14359	ST-865 complex	Blood	0.25	0.006	0.006	0.012
85560	England	2017/18	B	B	3526	ST-41/44 complex	Blood	0.125	0.004	0.008	0.004
85561	England	2017/18	B	B	1617	ST-22 complex	Blood	0.047	0.003	0.004	0.004
85564	England	2017/18	B	B	14360	ST-35 complex	Blood	0.094	0.125	0.003	0.004
85565	England	2017/18	B	B	461	ST-461 complex	Blood	0.19	0.006	0.003	0.006
85566	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.003	0.004
85567	England	2017/18	B	B	354	ST-269 complex	Blood	0.094	0.012	0.006	0.006
85568	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.002	0.002
85570	England	2017/18	B	B	14361	ST-461 complex	CSF	0.047	0.006	0.004	0.003
85573	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.38	0.064	0.004	0.012

85575	England	2017/18	C	C	11	ST-11 complex	Blood	0.064	0.032	0.004	0.004
85576	England	2017/18	W	W	114	ST-22 complex	Blood	0.064	0.012	0.004	0.004
85577	England	2017/18	B	B	1354	ST-269 complex	Blood	0.032	0.006	0.004	0.002
85578	England	2017/18	B	B	1194	ST-41/44 complex	Blood	0.047	0.006	0.004	0.003
85579	England	2017/18	B	B	3496	ST-213 complex	Blood	0.125	0.006	0.003	0.003
85580	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.25	0.008	0.004	0.004
85582	England	2017/18	B	B	485	ST-41/44 complex	Blood	0.125	0.008	0.004	0.004
85583	England	2017/18	B	B	14362	ST-461 complex	Blood	0.19	0.012	0.002	0.006
85584	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.19	0.008	0.002	0.003
85585	England	2017/18	Y	Y	1466	ST-174 complex	Blood	0.094	0.064	0.002	0.004
85587	England	2017/18	B	B	275	ST-269 complex	Blood	0.125	0.004	0.004	0.006
85588	England	2017/18	B	B	162	ST-162 complex	Blood	0.064	0.012	0.004	0.003
85589	England	2017/18	B	B	41	ST-41/44 complex	Blood	0.047	0.012	0.004	0.002
85591	England	2017/18	B	B	14363	UA	Blood	0.25	0.004	0.004	0.004
85592	Northern Ireland	2017/18	B	B	162	ST-162 complex	Blood	0.047	0.006	0.003	0.002
85593	England	2017/18	B	B	6798	UA	Blood	0.064	0.012	0.004	0.003
85594	England	2017/18	B	B	1161	ST-269 complex	Blood	0.19	0.012	0.003	0.003
85595	England	2017/18	B	B	11621	UA	Blood	0.032	0.006	0.003	<0.002
85596	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.003	0.003
85597	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.002	0.002
85598	England	2018/19	B	B	4713	UA	Blood	0.064	0.006	0.004	0.006
85600	England	2018/19	Y	Y	23	ST-23 complex	Blood	0.094	0.002	0.002	0.004
85601	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.19	0.006	0.004	0.003
85602	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.19	0.006	0.004	0.003
85603	England	2018/19	B	B	1161	ST-269 complex	Blood	0.5	0.006	0.003	0.004
85604	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.19	0.004	0.003	0.004
85605	England	2018/19	B	B	14364	ST-41/44 complex	Blood	0.125	0.006	0.004	0.003
85606	England	2018/19	B	B	4237	ST-865 complex	Blood	0.25	0.003	0.004	0.002
85623	England	2011/12	B	B	41	ST-41/44 complex	Blood	0.016	0.003	0.003	<0.002
89259	England	2018/19	B	B	230	ST-32 complex	Blood	0.064	0.023	0.18	0.003
94200	England	2017/18	B	B	282	ST-282 complex	Blood	0.125	0.032	0.006	0.008
94243	England	2017/18	B	B	1161	ST-269 complex	Blood	0.19	0.006	0.004	0.004
94245	England	2017/18	B	B	12656	ST-41/44 complex	Blood	0.19	0.006	0.003	0.004
94261	England	2017/18	B	B	13095	ST-32 complex	Blood	0.38	0.008	0.004	0.004
94263	England	2017/18	B	B	22	ST-22 complex	Blood	0.19	0.004	0.003	0.004
94265	England	2017/18	Y	Y	1655	ST-23 complex	Blood	0.032	0.004	0.003	0.002
94266	England	2018/19	B	B	1157	ST-1157 complex	Blood	0.047	0.006	0.003	0.003
94267	England	2018/19	B	B	2506	ST-32 complex	Blood	0.25	0.004	0.004	0.004
94268	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.047	0.004	0.004	0.002
94270	England	2018/19	B	B	269	ST-269 complex	Blood	0.125	0.006	0.004	<0.002
94275	England	2018/19	B	B	15214	ST-41/44 complex	Blood	0.047	0.003	0.004	<0.002
94277	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.002
94278	England	2018/19	B	B	639	ST-32 complex	Blood	0.047	0.047	0.004	0.002
94280	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.023	0.003	0.004	0.002
94281	Wales	2018/19	B	B	5151	UA	Blood	0.19	0.006	0.004	0.004
94283	England	2018/19	Y	Y	23	ST-23 complex	Blood	0.064	0.006	0.004	0.003
94284	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.19	0.008	0.004	0.003
94287	England	2018/19	Y	Y	10730	ST-167 complex	Blood	0.064	0.003	0.004	0.004
94288	Wales	2018/19	B	B	162	ST-162 complex	CSF	0.064	0.006	0.006	0.003
94290	England	2018/19	B	B	1992	ST-41/44 complex	Blood	0.19	0.023	0.004	0.003
94291	England	2018/19	B	B	15209	UA	Blood	0.25	0.012	0.004	0.006
94292	England	2018/19	C	C	11	ST-11 complex	Blood Culture	0.125	0.125	0.004	0.006
94293	England	2018/19	B	B	485	ST-41/44 complex	Blood Culture	0.19	0.006	0.004	0.004
94294	England	2018/19	B	B	3122	ST-213 complex	Blood	0.094	0.012	0.004	0.003
94296	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.064	0.006	0.004	0.003
94297	England	2018/19	B	B	15215	UA	Blood	0.38	0.047	0.004	0.008
94298	Wales	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.003	0.003	0.003
94299	England	2018/19	B	B	13441	ST-213 complex	Blood	0.032	0.016	0.003	<0.002
94300	England	2018/19	B	B	213	ST-213 complex	Blood	0.016	0.004	0.003	<0.002
94301	England	2018/19	B	B	1163	ST-269 complex	Blood	0.064	0.004	0.003	0.003
94302	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.125	0.002	0.004	0.004
94303	England	2018/19	B	B	5151	UA	Blood	0.125	0.004	0.004	0.004
94305	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.003
94306	England	2018/19	C	C	11	ST-11 complex	Blood Culture	0.047	0.047	0.006	0.003
94307	England	2018/19	B	B	1161	ST-269 complex	Blood Culture	0.19	0.004	0.004	0.002
94393	England	2018/19	C	C	15210	ST-41/44 complex	Blood Culture	0.023	0.008	0.006	0.002
94395	England	2018/19	Y	Y	11866	ST-23 complex	Blood	0.047	0.004	0.004	0.004
94398	England	2018/19	Y	Y	23	ST-23 complex	Blood	0.125	0.004	0.004	0.008
94399	England	2018/19	B	B	33	ST-32 complex	Blood	0.064	0.004	0.004	0.002
94400	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.064	0.004	0.004	0.004
94401	England	2018/19	B	B	9293	ST-162 complex	Blood	0.125	0.012	0.008	0.004
94402	England	2018/19	B	B	4713	UA	Blood	0.064	0.006	0.008	0.006
94403	England	2018/19	Y	Y	6463	ST-23 complex	Blood	0.094	0.012	0.008	0.004
94404	England	2018/19	C	C	485	ST-41/44 complex	Blood	0.25	0.008	0.008	0.006
94406	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.094	0.006	0.004	0.003
94407	England	2018/19	B	B	15216	UA	Blood	0.064	0.003	0.004	0.003
94408	England	2018/19	Y	Y	12176	ST-23 complex	Blood	0.064	0.003	0.004	0.004
94409	England	2018/19	Y	Y	23	ST-23 complex	Joint	0.38	0.003	0.004	0.004
94410	England	2018/19	B	B	15211	UA	Blood	0.032	0.016	0.003	<0.002
94411	England	2018/19	B	B	269	ST-269 complex	Blood	0.047	0.004	0.006	0.003
94412	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.047	0.003	0.004	0.004
94413	England	2018/19	B	B	1163	ST-269 complex	Blood	0.38	0.006	0.006	0.016
94415	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.032	0.003	0.004	0.003
94418	England	2018/19	C	C	11	ST-11 complex	Blood	0.094	0.032	0.006	0.004
94419	England	2018/19	C	C	11	ST-11 complex	Blood	0.064	0.023	0.008	0.012

94420	England	2018/19	B	B	41	ST-41/44 complex	Blood	0.047	0.008	0.008	0.003
94423	England	2018/19	Y	NK	1655	ST-23 complex	Blood	0.064	0.006	0.006	0.006
94449	England	2018/19	B	B	213	ST-213 complex	Blood	0.047	0.008	0.004	0.003
94450	Wales	2018/19	B	B	10297	UA	Blood	0.094	0.032	0.004	0.004
94451	England	2018/19	B	B	213	ST-213 complex	Blood	0.023	0.032	0.004	<0.002
94452	England	2018/19	B	B	485	ST-41/44 complex	Blood	0.19	0.012	0.006	0.004
94453	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.064	0.008	0.006	0.004
94454	England	2018/19	B	B	479	ST-269 complex	Blood	0.047	0.012	0.004	0.002
94455	England	2018/19	B	B	1163	ST-269 complex	Brain	0.19	0.004	0.003	0.004
94457	England	2018/19	B	B	11238	ST-269 complex	Blood	0.094	0.016	0.006	0.004
94464	England	2018/19	Y	Y	1655	ST-23 complex	Blood	0.094	0.004	0.004	0.003
94466	England	2018/19	B	B	2314	ST-41/44 complex	Blood	0.25	0.008	0.006	0.004
94467	England	2018/19	C	C	11	ST-11 complex	Blood	0.125	0.006	0.008	0.006
94468	England	2018/19	B	B	41	ST-41/44 complex	Blood	0.125	0.006	0.008	0.004
94469	England	2018/19	B	B	33	ST-32 complex	Blood	0.047	0.006	0.006	0.003
19968*	England	2010/11	W	W	11	ST-11 complex	Blood	0.094	0.023	0.004	0.006
20057*	England	2010/11	W	W	11	ST-11 complex	Blood	0.38	0.012	0.006	0.004
20154*	England	2010/11	W	W	11	ST-11 complex	Blood	0.064	0.006	0.003	0.004
20158*	England	2010/11	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.004
20216*	England	2010/11	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.003
20226*	England	2010/11	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.003
20247*	England	2010/11	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.002
20288*	England	2010/11	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
20368*	England	2010/11	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.004
20424*	England	2010/11	W	W	11	ST-11 complex	Joint	0.094	0.004	0.004	0.006
20436*	England	2010/11	W	W	11	ST-11 complex	Blood	0.064	0.008	0.003	0.003
20449*	England	2010/11	W	W	11	ST-11 complex	Blood	0.094	0.006	0.004	0.004
20460*	England	2011/12	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.004
20461*	England	2011/12	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.006
21123*	England	2011/12	W	W	1860	ST-11 complex	Blood	0.064	0.008	0.004	0.004
21163*	England	2011/12	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.004
21206*	England	2011/12	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.004
21216*	England	2011/12	W	W	11	ST-11 complex	Blood	0.032	0.006	0.003	0.003
21298*	England	2011/12	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
21302*	England	2011/12	W	W	11	ST-11 complex	Blood	0.047	0.004	0.006	0.003
21305*	England	2011/12	W	W	11	ST-11 complex	Blood	0.094	0.004	0.006	0.004
21334*	England	2011/12	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.003
21354*	England	2011/12	W	W	11	ST-11 complex	Blood	0.064	0.006	0.006	0.004
21375*	England	2011/12	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.004
21377*	England	2011/12	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.004
21381*	England	2011/12	W	W	11	ST-11 complex	Blood	0.047	0.004	0.006	0.004
21386*	England	2011/12	W	W	10284	ST-11 complex	Blood	0.064	0.008	0.004	0.006
21446*	England	2011/12	W	W	11	ST-11 complex	Blood	0.047	0.032	0.006	0.003
21492*	England	2011/12	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.002
28114*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.016	0.008	0.003
28115*	England	2012/13	W	W	11	ST-11 complex	Blood	0.032	<0.002	0.008	<0.002
28116*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.003
28117*	England	2012/13	W	W	11	ST-11 complex	Blood	0.38	0.012	0.004	0.006
28119*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.006	0.008	0.003
28122*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.003	0.003	0.003
28125*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.004	0.002	0.003
28128*	England	2012/13	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.004
28131*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.006	0.003	0.004
28132*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.006	0.003	0.004
28134*	England	2012/13	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.003
28135*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.012	0.003	0.003
28136*	England	2012/13	W	W	11	ST-11 complex	Blood	0.094	0.008	0.003	0.004
28137*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.008	0.003	0.004
28138*	England	2012/13	W	W	11	ST-11 complex	Blood	0.38	0.016	0.004	0.012
28139*	England	2012/13	W	W	10651	ST-11 complex	Blood	0.047	0.006	0.003	0.003
28141*	England	2012/13	W	W	11	ST-11 complex	Blood	0.094	0.012	0.004	0.004
28142*	England	2012/13	W	W	11	ST-11 complex	Blood	0.094	0.008	0.004	0.004
28143*	England	2012/13	W	W	11	ST-11 complex	Blood	0.094	0.008	0.008	0.004
28144*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.006	0.003	0.003
28146*	England	2012/13	W	W	10651	ST-11 complex	Blood	0.064	0.006	0.002	0.004
28147*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.012	0.003	0.004
28149*	England	2012/13	W	W	11	ST-11 complex	Joint	0.047	0.008	0.003	0.004
28150*	England	2012/13	W	W	11	ST-11 complex	Blood	0.032	0.008	0.003	0.003
28151*	England	2012/13	W	W	11	ST-11 complex	Blood	0.047	0.012	0.003	0.003
28152*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.008	0.003	0.003
28153*	England	2012/13	W	W	11	ST-11 complex	Blood	0.047	0.006	0.006	0.004
28154*	England	2012/13	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.003
28156*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.004	0.006	0.004
28157*	England	2012/13	W	W	11	ST-11 complex	Blood	0.047	0.004	0.008	0.003
28158*	England	2012/13	W	W	11	ST-11 complex	Blood	0.094	0.012	0.012	0.006
28161*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.008	0.008	0.003
28162*	England	2012/13	W	W	11	ST-11 complex	Blood	0.094	0.006	0.012	0.004
28163*	England	2012/13	W	W	11	ST-11 complex	Blood	0.047	0.016	0.006	0.006
28164*	England	2012/13	W	W	11	ST-11 complex	Blood	0.064	0.002	0.008	0.004
29721*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.004	0.008	0.004
29723*	England	2013/14	W	W	11	ST-11 complex	Blood	0.125	0.008	0.008	0.012
29724*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.004
29725*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.006	0.006	0.006
29726*	England	2013/14	W	W	10651	ST-11 complex	Blood	0.064	0.004	0.006	0.004
29728*	England	2013/14	W	W	11	ST-11 complex	Blood	0.094	0.006	0.006	0.004

29729*	England	2013/14	W	W	11	ST-11 complex	Blood	0.094	0.008	0.008	0.006
29730*	England	2013/14	W	W	11161	ST-11 complex	Blood	0.064	0.016	0.008	0.006
29731*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.006	0.008	0.004
29732*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.004	0.006	0.006
29733*	England	2013/14	W	W	11	ST-11 complex	Blood	0.094	0.008	0.008	0.004
29734*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.004	0.008	0.006
29735*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.008	0.006	0.004
29736*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.008	0.006	0.004
29737*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.006	0.006	0.006
30136*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.006	0.008	0.004
30137*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.004
30138*	England	2013/14	W	W	11	ST-11 complex	Blood	0.094	0.008	0.008	0.008
30139*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.006	0.008	0.008
30140*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.004
30141*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.004
30143*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.016	0.006	0.004
30144*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.016	0.006	0.004
30145*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.003	0.008	0.003
30146*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.023	0.008	0.004
30147*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.004
30148*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.004
30150*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.003	0.004	0.004
30151*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.004	0.006	0.004
30152*	England	2013/14	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.004
30153*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.003	0.006	0.003
30154*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.004
30155*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.012	0.006	0.004
30156*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.016	0.008	0.006
30157*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.008	0.006	0.006
30158*	England	2013/14	W	W	11	ST-11 complex	Blood	0.125	0.023	0.006	0.008
30159*	England	2013/14	W	W	8621	ST-11 complex	Blood	0.064	0.016	0.006	0.006
30160*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.004
30161*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.006
30162*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.006
30163*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.016	0.004	0.006
30164*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.006
30165*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.023	0.006	0.004
30166*	England	2013/14	W	W	10651	ST-11 complex	Blood	0.094	0.008	0.008	0.006
30167*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.008	0.008	0.006
30168*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.004	0.006	0.006
31168*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.003
31169*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.003	0.006	0.004
35425*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.125	0.016	0.004
35507*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.047	0.008	0.004
35581*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.008	0.008	0.008
35598*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.006	0.008	0.004
35608*	England	2013/14	W	NG	11	ST-11 complex	Blood	0.047	0.006	0.012	0.004
35614*	England	2013/14	W	W	11	ST-11 complex	Blood	0.032	0.004	0.008	0.004
35618*	England	2013/14	W	W	11	ST-11 complex	CSF	0.064	0.008	0.012	0.006
35621*	England	2013/14	W	W	11	ST-11 complex	Blood	0.094	0.012	0.012	0.012
35622*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.016	0.008	0.008
35624*	England	2013/14	W	W	11	ST-11 complex	Blood	0.094	0.012	0.012	0.008
35632*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.004	0.006	0.008
35634*	England	2013/14	W	W	11	ST-11 complex	Blood	0.032	0.008	0.006	0.004
35635*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.023	0.008	0.008
35638*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.006
35643*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.016	0.006	0.006
35651*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.008	0.006	0.006
35664*	England	2013/14	W	W	11292	ST-11 complex	Blood	0.064	0.012	0.006	0.008
35670*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.008
35674*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.006
35675*	England	2013/14	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.003
35686*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.006
35687*	England	2013/14	W	W	10651	ST-11 complex	Blood	0.125	0.016	0.006	0.012
35689*	England	2013/14	W	W	11	ST-11 complex	Blood	0.064	0.023	0.006	0.006
35690*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.004
35700*	England	2013/14	W	W	10651	ST-11 complex	Blood	0.064	0.012	0.006	0.006
35702*	England	2013/14	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.004
35722*	England	2013/14	W	W	11	ST-11 complex	Blood	0.125	0.032	0.008	0.008
35725*	England	2013/14	W	W	11	ST-11 complex	Blood	0.094	0.023	0.006	0.008
35728*	England	2013/14	W	W	11	ST-11 complex	Blood	0.094	0.016	0.006	0.006
35745*	England	2014/15	W	W	NK	INCOMPLETE MLST	Blood	0.064	0.016	0.008	0.006
35754*	England	2014/15	W	W	11	ST-11 complex	Blood	0.023	0.008	0.006	0.004
35756*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.008	0.006	0.004
35763*	England	2014/15	W	W	11	ST-11 complex	Blood	0.125	0.016	0.008	0.008
35782*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.012	0.006	0.004
35786*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.004
35788*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.004
35792*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.004
35796*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.008	0.006	0.004
35799*	England	2014/15	W	W	11	ST-11 complex	Joint	0.064	0.008	0.006	0.006
35800*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.016	0.006	0.003
35801*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.032	0.008	0.004
35807*	England	2014/15	W	W	10651	ST-11 complex	Blood	0.064	0.012	0.006	0.004
35808*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.012	0.006	0.004

35809*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
35810*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.003
35811*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.003
37670*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.012	0.006	0.004
37673*	England	2014/15	W	NK	10651	ST-11 complex	Blood	0.047	0.023	0.006	0.003
37675*	England	2014/15	W	NK	10651	ST-11 complex	Blood	0.064	0.006	0.008	0.004
37681*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.032	0.008	0.008	0.003
37685*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
37690*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.012	0.006	0.004
37692*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.006	0.006	0.004
37693*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.012	0.006	0.004
37699*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.032	0.004	0.004	0.002
37701*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.064	0.016	0.006	0.004
37708*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.006	0.006	0.004
37710*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.012	0.008	0.004
37711*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.004
37716*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.006	0.008	0.002
37717*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.032	0.006	0.006	0.004
37722*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.003	0.006	0.002
37731*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.003	0.004	0.002
37732*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.004
37736*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.004
37738*	England	2014/15	W	W	10651	ST-11 complex	Blood	0.047	0.012	0.006	0.004
37739*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.006	0.006	0.004
37742*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.008	0.006	0.004
37746*	England	2014/15	W	NK	11867	ST-11 complex	Blood	0.094	0.012	0.008	0.008
37747*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.006	0.008	0.002
37748*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.006	0.008	<0.002
37749*	England	2014/15	W	NK	10651	ST-11 complex	Blood	0.064	0.008	0.008	0.003
37754*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.012	0.008	0.004
37757*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.008	0.008	0.002
37760*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.004
37769*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.19	0.008	0.008	0.006
37770*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
37774*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.002
37784*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.064	0.006	0.006	0.004
37793*	England	2014/15	W	W	11	ST-11 complex	Blood	0.023	0.006	0.006	0.002
37797*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.38	0.023	0.008	0.016
37798*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.004	0.006	0.003
37799*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.006	0.006	0.002
37801*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.004	0.008	0.002
37805*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.008	0.008	0.003
37806*	England	2014/15	W	W	11	ST-11 complex	Blood	0.125	0.023	0.008	0.006
37809*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.004	0.006	0.004
37811*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.012	0.008	0.004
37821*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.125	0.012	0.002	0.002
37822*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.032	0.002	0.002	0.016
37828*	England	2014/15	W	W	11	ST-11 complex	Blood	0.094	0.004	0.002	0.016
37834*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.006	0.002	0.004
37854*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.012	0.002	0.006
37855*	England	2014/15	W	W	NK	INCOMPLETE MLST	Blood	0.094	0.023	0.002	0.008
37856*	England	2014/15	W	NG	11	ST-11 complex	Blood	0.047	0.008	0.002	0.004
37857*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.094	0.008	0.002	0.006
37860*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.032	0.006	0.002	0.004
37861*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.064	0.008	0.002	0.006
37862*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.006	0.002	0.004
37868*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.19	0.004	0.002	0.008
37870*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.004	0.002	0.004
37873*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.004	0.002	0.004
37875*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.004	0.002	0.004
37879*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.004	0.012	0.004
37881*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.004
37882*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.023	0.004	0.004	0.002
37890*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.064	0.016	0.008	0.006
37891*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.023	0.004	0.004	0.003
37893*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.008	0.006	0.006
37902*	England	2014/15	W	NK	10651	ST-11 complex	Blood	0.064	0.016	0.006	0.006
37904*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.064	0.012	0.008	0.006
37907*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.012	0.006	0.006
37910*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.064	0.012	0.006	0.004
37915*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.047	0.008	0.004
37922*	England	2014/15	W	NK	10651	ST-11 complex	Blood	0.047	0.008	0.006	0.004
37930*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.064	0.012	0.006	0.004
37933*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.032	0.012	0.006	0.002
37936*	England	2014/15	W	NK	11	ST-11 complex	Joint	0.047	0.012	0.006	0.004
37940*	England	2014/15	W	W	11	ST-11 complex	Joint	0.047	0.006	0.008	0.004
37942*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.032	0.012	0.006	0.004
37951*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.023	0.004	0.004	0.002
37958*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.006	0.006	0.002
37961*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.006	0.008	0.004
37962*	England	2014/15	W	NK	NK	INCOMPLETE MLST	Blood	0.064	0.016	0.008	0.004
37977*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.002
37978*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.016	0.006	0.004
37981*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.094	0.016	0.008	0.008
37983*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.003	0.004	0.002

37987*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.006	0.006	0.002
37988*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.004	0.006	0.002
37990*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.004
37992*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.004	0.006	0.002
37995*	England	2014/15	W	W	11	ST-11 complex	CSF	0.064	0.008	0.008	0.003
37998*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.016	0.008	0.002
37999*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.064	0.008	0.002
38001*	England	2014/15	W	W	10651	ST-11 complex	Blood	0.064	0.012	0.008	0.003
38003*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.012	0.008	0.003
38004*	England	2014/15	W	W	11	ST-11 complex	Blood	0.094	0.047	0.008	0.004
38007*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.008	0.008	0.003
38008*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.094	0.008	0.003
38017*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.064	0.008	0.008	0.002
38024*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.094	0.012	0.008	0.004
38027*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
38029*	England	2014/15	W	W	NK	INCOMPLETE MLST	Joint	0.064	0.023	0.008	0.004
38034*	England	2014/15	W	W	11	ST-11 complex	Blood	0.094	0.012	0.004	0.006
38035*	England	2014/15	W	W	NK	INCOMPLETE MLST	Blood	0.047	0.008	0.004	0.002
38037*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.003
38038*	England	2014/15	W	W	11	ST-11 complex	Blood	0.094	0.008	0.008	0.006
38049*	England	2014/15	W	NK	11	ST-11 complex	Joint	0.094	0.012	0.008	0.006
38059*	England	2014/15	W	W	10651	ST-11 complex	Joint	0.094	0.016	0.004	0.004
38060*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.032	0.008	0.004	0.008
38063*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
38064*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.064	0.008	0.004	0.004
38065*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.003	0.004	0.002
38066*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.004
38067*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.064	0.016	0.004	0.004
38076*	England	2014/15	W	W	11	ST-11 complex	Blood	0.094	0.012	0.004	0.004
38079*	England	2014/15	W	W	11	ST-11 complex	Blood	0.094	0.008	0.008	0.004
38085*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.094	0.012	0.004	0.003
38088*	England	2014/15	W	NK	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
38096*	England	2014/15	W	W	11491	ST-11 complex	Blood	0.064	0.012	0.004	0.002
38101*	England	2014/15	W	NK	11	ST-11 complex	Joint	0.064	0.008	0.004	0.002
38102*	England	2014/15	W	W	NK	INCOMPLETE MLST	Blood	0.064	0.012	0.004	0.003
38106*	England	2014/15	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.003
38108*	England	2014/15	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
38109*	England	2014/15	W	W	11	ST-11 complex	Joint	0.064	0.008	0.004	0.003
38115*	England	2014/15	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.003
38520*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.006	0.008	0.002
39320*	England	2015/16	W	W	11	ST-11 complex	Blood	0.25	0.006	0.004	0.004
39328*	England	2015/16	W	W	11	ST-11 complex	Joint	0.064	0.016	0.004	0.004
39331*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
39335*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.012	0.008	0.003
39337*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
39340*	England	2015/16	W	W	11	ST-11 complex	Blood	0.19	0.032	0.008	0.008
39341*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.002
39342*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.008	0.008	0.003
39344*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.006	0.008	0.003
39345*	England	2015/16	W	NK	11	ST-11 complex	Blood	0.064	0.006	0.008	0.003
39346*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.012	0.008	0.003
39349*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.047	0.012	0.003	0.008
39352*	England	2015/16	W	W	11	ST-11 complex	Joint	0.047	0.006	0.008	0.002
39356*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
39358*	England	2015/16	W	W	11	ST-11 complex	Blood	0.032	0.008	0.004	0.002
39365*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.016	0.008	0.003
39368*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.002
39369*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.25	0.008	0.002
39373*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.064	0.008	0.003
39385*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.006	0.008	0.003
39395*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.023	0.008	0.004
39396*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.094	0.008	0.004
39398*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.004	0.004	0.003
39401*	England	2015/16	W	W	11	ST-11 complex	CSF	0.047	0.008	0.004	0.003
39404*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.003
39408*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.008
39410*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.004	0.002	0.008
39411*	England	2015/16	W	W	11	ST-11 complex	Blood	0.004	0.012	0.004	0.008
39412*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.012	0.003	0.008
39421*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.003	0.004	0.002
39423*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
39427*	England	2015/16	W	W	11	ST-11 complex	Joint	0.047	0.006	0.004	0.003
39429*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
39430*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.023	0.008	0.004
39431*	England	2015/16	W	W	11	ST-11 complex	Blood	0.125	0.023	0.008	0.004
39433*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.008	0.004	0.003
39435*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.094	0.008	0.003
39436*	England	2015/16	W	W	11	ST-11 complex	CSF	0.064	0.004	0.008	0.003
39438*	England	2015/16	W	W	11	ST-11 complex	Blood	0.125	0.008	0.008	0.004
40322*	England	2015/16	W	W	11	ST-11 complex	Blood	0.125	0.012	0.004	0.003
41451*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.19	0.008	0.002
41455*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.003
41462*	England	2015/16	W	W	11	ST-11 complex	Blood	0.125	0.008	0.004	0.003
41463*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.004	0.004	0.003
41467*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.19	0.008	0.004

41469*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.003
41470*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.016	0.008	0.003
41473*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.004	0.004	0.002
41478*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.008	0.004	0.003
41481*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.003	0.004	0.002
41483*	England	2015/16	NG	W	11	ST-11 complex	Blood	0.094	0.016	0.008	0.004
41486*	England	2015/16	W	W	11	ST-11 complex	Blood	0.125	0.016	0.004	0.004
41489*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.094	0.006	0.004	0.004
41494*	England	2015/16	W	W	11	ST-11 complex	CSF	0.094	0.008	0.004	0.004
41501*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.002
41502*	England	2015/16	W	W	11	ST-11 complex	Joint	0.094	0.008	0.006	0.004
41515*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.012	0.004	0.006
41516*	England	2015/16	W	W	11	ST-11 complex	Blood	0.023	0.006	0.002	0.002
41519*	England	2015/16	W	NK	11	ST-11 complex	Joint	0.094	0.047	0.008	0.004
41522*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.004	0.003	0.002
41525*	England	2015/16	W	W	11	ST-11 complex	Blood	0.023	0.006	0.004	0.002
41530*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.012	0.006	0.004
41531*	England	2015/16	W	W	11	ST-11 complex	CSF	0.064	0.006	0.004	0.003
41533*	England	2015/16	W	W	10651	ST-11 complex	Blood	0.064	0.012	0.004	0.003
41536*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.047	0.004	0.004	0.002
41543*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.016	0.006	0.004
41547*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
41549*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
41552*	England	2015/16	W	W	10651	ST-11 complex	Blood	0.094	0.008	0.006	0.006
41558*	England	2015/16	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.003
42475*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.016	0.006	0.003
42476*	England	2015/16	W	W	10651	ST-11 complex	Blood	0.094	0.012	0.008	0.003
42478*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	<0.002
42480*	England	2015/16	W	NK	11	ST-11 complex	Blood	0.047	0.006	0.004	<0.002
42481*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.012	0.004	0.003
42482*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.012	0.006	0.003
42483*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.008	0.008	0.003
42484*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
42485*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.003
42486*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
42489*	England	2015/16	W	NK	11	ST-11 complex	Blood	0.064	0.008	0.004	0.004
42491*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.047	0.008	0.006	<0.002
42492*	England	2015/16	W	W	11	ST-11 complex	Blood	0.032	0.012	0.004	<0.002
42494*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.002	0.004	0.002
42497*	England	2015/16	W	W	10651	ST-11 complex	Blood	0.064	0.006	0.006	0.003
42504*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.032	0.016	0.004	<0.002
42505*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.064	0.006	0.004	0.003
42506*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.047	0.006	0.004	0.003
42512*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.047	0.006	0.008	<0.002
42517*	England	2015/16	W	NK	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
42519*	England	2015/16	W	NK	11	ST-11 complex	Joint	0.047	0.004	0.004	0.003
42525*	England	2015/16	W	W	10651	ST-11 complex	Blood	0.094	0.012	0.004	0.003
42530*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.006
42532*	England	2015/16	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.003
42533*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.008	0.004	0.006
42534*	England	2015/16	W	W	NK	UA	Blood	0.094	0.012	0.004	0.006
42535*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.008	0.002	0.002
42545*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.004	0.004	0.006
42549*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.004	0.006	0.006
42551*	England	2015/16	W	NK	11	ST-11 complex	Blood	0.047	0.008	<0.002	<0.002
42552*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	<0.002
42553*	England	2015/16	W	W	11	ST-11 complex	Blood	0.19	0.006	0.004	0.002
42555*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.012	0.004	0.006
42556*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.004	0.006	<0.002
42561*	England	2015/16	W	W	10651	ST-11 complex	Blood	0.064	0.016	0.004	0.003
42564*	England	2015/16	W	W	11	ST-11 complex	Blood	0.032	0.064	0.004	0.002
42568*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
42572*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.003
42573*	England	2015/16	W	W	10651	ST-11 complex	Blood	0.047	0.012	0.004	0.003
42576*	England	2015/16	W	NK	11	ST-11 complex	Blood	0.032	0.003	0.004	0.002
42585*	England	2015/16	W	W	11	ST-11 complex	Joint	0.047	0.006	0.006	0.003
42586*	England	2015/16	W	W	10651	ST-11 complex	Blood	0.064	0.012	0.004	0.004
42595*	England	2015/16	W	NK	11	ST-11 complex	Blood	0.38	0.012	0.004	0.004
42605*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.016	0.004	0.003
42612*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.016	0.004	0.006
44636*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.004	0.003	0.002
44638*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.003	0.008	0.004
44640*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.002
44684*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.023	0.004	0.003
44685*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.008	0.003	0.003
44686*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.003	0.004	0.003
44687*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.004
44697*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.094	0.012	0.006	0.003
44699*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.064	0.003	0.004	0.003
44704*	England	2015/16	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
44708*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.004	0.004	0.004
44714*	England	2015/16	W	W	8621	ST-11 complex	Blood	0.094	0.012	0.004	0.004
44718*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.016	0.004	0.003
44719*	England	2015/16	W	W	11	ST-11 complex	Blood	0.032	0.008	0.004	0.002
44721*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.004

44724*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.008	0.006	0.003
44727*	England	2015/16	W	W	10651	ST-11 complex	Joint	0.094	0.016	0.006	0.004
44730*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
44733*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.003
44736*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.004
44739*	England	2015/16	W	W	11	ST-11 complex	Blood	0.032	0.003	0.004	<0.002
44740*	England	2015/16	W	NK	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
44742*	England	2015/16	W	W	12208	ST-11 complex	Blood	0.023	0.032	0.008	0.002
44753*	England	2015/16	W	W	11	ST-11 complex	Joint	0.094	0.008	0.003	0.004
44759*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.008	0.004	0.003
44763*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.008	0.004	0.002
44765*	England	2015/16	W	W	11	ST-11 complex	Joint	0.094	0.012	0.004	0.002
44768*	England	2015/16	W	W	11	ST-11 complex	Blood	0.125	0.012	0.008	0.004
44769*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.047	0.006	0.003
44773*	England	2015/16	W	W	11	ST-11 complex	Blood	0.094	0.125	0.008	0.003
44777*	England	2015/16	W	W	11	ST-11 complex	Blood	0.25	0.125	0.008	0.008
44782*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.047	0.008	0.004	0.003
44784*	England	2015/16	W	W	NK	INCOMPLETE MLST	Joint	0.064	0.012	0.004	0.003
44785*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.047	0.006	0.006	0.003
44786*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.064	0.012	0.008	0.004
44788*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.064	0.064	0.004	0.004
44790*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.094	0.012	0.006	0.006
44798*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.047	0.19	0.008	0.004
44802*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.094	0.012	0.006	0.004
44828*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.125	0.008	0.003
44829*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.064	0.012	0.006	0.003
44833*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.032	0.004	0.004	0.003
44835*	England	2015/16	W	W	NK	INCOMPLETE MLST	Blood	0.047	0.008	0.004	0.002
47016*	England	2015/16	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.004
47019*	England	2015/16	W	W	11	ST-11 complex	Blood	0.125	0.016	0.004	0.004
47262*	England	2015/16	W	W	11	ST-11 complex	Blood	0.032	0.006	0.006	0.002
47263*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.012	0.006	0.003
47265*	England	2015/16	W	W	11	ST-11 complex	Blood	0.047	0.004	0.008	<0.002
47271*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.008	0.008	0.003
47273*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
47274*	England	2016/17	W	W	10651	ST-11 complex	Blood	0.064	0.012	0.004	0.003
47275*	England	2016/17	W	W	10651	ST-11 complex	Blood	0.064	0.008	0.004	0.004
47277*	England	2016/17	W	W	10651	ST-11 complex	Blood	0.094	0.006	0.004	0.004
47280*	England	2016/17	W	W	10215	ST-11 complex	Blood	0.047	0.023	0.002	0.004
47287*	England	2016/17	W	W	12511	ST-11 complex	Blood	0.047	0.004	0.004	0.003
47289*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.003
47294*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.006	0.008	0.008
47296*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.023	0.006	0.003
47299*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.012	0.006	0.006
47301*	England	2016/17	W	W	11	ST-11 complex	Blood	0.023	0.003	0.004	0.002
47303*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.006	0.003
47304*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.003
47305*	England	2016/17	W	NK	11	ST-11 complex	Blood	0.032	0.006	0.008	0.002
47311*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.003
47322*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.012	0.008	0.004
47325*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.003
47326*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	<0.002
47329*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.008	0.006	0.004
47334*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.008	0.004	0.003
47336*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.003
47337*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.004
47338*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.012	0.006	0.003
47340*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
53050*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.12	0.004	0.003
53053*	England	2016/17	W	W	10651	ST-11 complex	Blood	0.064	0.006	0.006	0.004
53054*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
53056*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.003	0.008	0.003
53058*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
53060*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.006	0.003
53064*	England	2016/17	W	W	10651	ST-11 complex	Blood	0.064	0.016	0.006	0.003
53067*	England	2016/17	W	W	11	ST-11 complex	CSF	0.064	0.012	0.004	0.004
53069*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.002
53072*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.125	0.008	0.003
53074*	England	2016/17	W	W	10651	ST-11 complex	Blood	0.094	0.012	0.008	0.006
53076*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.003
53078*	England	2016/17	W	W	11	ST-11 complex	Blood	0.023	0.004	0.004	0.003
53080*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.003
53081*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.002
53082*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.002
53084*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.016	0.004	0.004
53086*	England	2016/17	W	W	11	ST-11 complex	Joint	0.064	0.008	0.004	0.008
53091*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.003	0.004	0.002
53092*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.002
53093*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.032	0.004	0.004
53096*	England	2016/17	W	W	11	ST-11 complex	Blood	0.125	0.008	0.004	0.002
53110*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.064	0.004	0.004
53113*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.003
53119*	England	2016/17	W	W	11	ST-11 complex	Blood	0.38	0.064	0.004	0.004
53121*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.008	0.008	0.006
53123*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.008	0.008	0.003

53133*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.023	0.004	0.003
53135*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
53139*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.003	0.004	0.003
53141*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
53142*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
53143*	England	2016/17	W	W	11	ST-11 complex	Joint	0.032	0.003	0.004	0.002
53146*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
53149*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
53150*	England	2016/17	W	W	1287	ST-11 complex	Blood	0.047	0.016	0.004	0.003
53154*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.003
53159*	England	2016/17	W	W	13099	ST-11 complex	Blood	0.064	0.032	0.004	0.004
53164*	England	2016/17	W	W	11	ST-11 complex	Joint	0.25	0.008	0.004	0.004
53165*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.004	0.008	0.003
53166*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.016	0.004	0.003
53167*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.003
53170*	England	2016/17	W	W	11	ST-11 complex	Blood	0.125	0.023	0.008	0.006
53176*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.008	0.003
53179*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.008	0.003
53183*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.003	0.008	0.004
53188*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.016	0.008	0.003
53190*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.008	0.003
53192*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.002
53194*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.004
53195*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.002
53196*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.002
53198*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.002
53199*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.003
53200*	England	2016/17	W	W	11	ST-11 complex	Blood	0.125	0.004	0.008	0.004
53208*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.016	0.008	0.006
53212*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.008	0.002
53213*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.008	0.003
53215*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.004	0.008	0.006
53217*	England	2016/17	W	NK	11	ST-11 complex	Blood	0.047	0.006	0.008	0.004
53222*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.012	0.008	0.006
53226*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.008	0.002
53230*	England	2016/17	W	W	11	ST-11 complex	Blood	0.25	0.006	0.008	0.006
53231*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.008	0.004
53232*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.003
53233*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.003
53236*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.008	0.002
53237*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.003
53244*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.004
53249*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.008	0.003
53252*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.012	0.008	0.004
53255*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.006	0.008	0.004
53256*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.008	0.003
53259*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.008	0.002
53264*	England	2016/17	W	W	11	ST-11 complex	Joint	0.047	0.003	0.008	0.002
53267*	England	2016/17	W	W	11	ST-11 complex	Blood	0.19	0.008	0.008	0.004
53269*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.016	0.008	0.003
53270*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.003	0.004	0.002
53274*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.19	0.004	0.003
53275*	England	2016/17	W	W	11	ST-11 complex	Blood	0.023	0.002	0.004	0.002
53279*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
53284*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.016	0.004	0.003
53287*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
53291*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.004
53292*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.008	0.004	0.002
53296*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.016	0.008	0.004
53297*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.023	0.004	0.002
53300*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.008	0.003
53301*	England	2016/17	NG	W	11	ST-11 complex	Blood	0.047	0.023	0.008	0.003
53307*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.125	0.008	0.004
53308*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.003	0.004	0.003
53309*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.008	0.003
53315*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.008	0.003
53322*	England	2016/17	W	W	11	ST-11 complex	Blood	0.023	0.004	0.004	0.002
53323*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.004
53325*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.002
53328*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.012	0.008	0.003
53338*	England	2016/17	W	W	11	ST-11 complex	Blood	0.023	0.006	0.004	<0.002
53339*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.004
53340*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
53341*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
53343*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.003
53344*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
53346*	England	2016/17	W	W	13097	ST-11 complex	Blood	0.064	0.023	0.008	0.006
53347*	England	2016/17	W	W	11	ST-11 complex	Blood	0.19	0.006	0.008	0.006
53350*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
53352*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.008	0.004	0.002
53354*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.008	0.004	0.003
53355*	England	2016/17	W	W	11	ST-11 complex	Blood	0.023	0.003	0.004	<0.002
53358*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.004
53360*	England	2016/17	W	W	11	ST-11 complex	Blood	0.023	0.008	0.004	0.002
53365*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.003

53367*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.003
53368*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.016	0.008	0.004
53369*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.003	0.004	0.003
53371*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.003
53372*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.004
60544*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
60545*	England	2017/18	W	W	11	ST-11 complex	Blood	0.19	0.008	0.006	0.004
60549*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
60552*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.004
60553*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.004
60555*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.002
60557*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
60558*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
60562*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.003	0.004	0.002
60565*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.032	0.006	0.006
60572*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.002
60579*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.002
60587*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
60589*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.004	0.004	0.006
60590*	England	2017/18	W	W	11	ST-11 complex	Blood	0.023	0.012	0.004	<0.002
60591*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
60592*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
60597*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.19	0.003	0.003
60601*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.016	0.004	0.004
60603*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.012	0.008	0.004
60612*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
60613*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.016	0.006	0.003
60614*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.003	0.004	0.003
60619*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
60631*	England	2017/18	W	W	11	ST-11 complex	Blood	0.38	0.016	0.004	0.006
60632*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.002
60642*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.016	0.006	0.004
60645*	England	2016/17	W	W	11	ST-11 complex	Blood	0.125	0.004	0.008	0.004
60649*	England	2017/18	W	W	11	ST-11 complex	Joint	0.064	0.004	0.006	0.003
60657*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
60663*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.003
60671*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.004	0.006	0.003
60672*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.003
60674*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.003
60675*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
60676*	England	2017/18	W	W	NK	INCOMPLETE MLST	Blood	0.016	0.008	0.004	<0.002
60681*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.006
60682*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.003
60685*	England	2016/17	W	W	NK	INCOMPLETE MLST	Blood	0.125	0.032	0.008	0.004
60692*	England	2017/18	W	W	11	ST-11 complex	Blood	0.023	0.012	0.004	0.002
60694*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.003
60699*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.032	0.006	0.003
60700*	England	2016/17	W	W	11	ST-11 complex	Blood	0.094	0.016	0.004	0.008
60706*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
60707*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
60708*	England	2016/17	W	W	11	ST-11 complex	Joint	0.38	0.032	0.008	0.006
60710*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.004
60718*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.016	0.008	0.002
60720*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
60723*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.032	0.008	0.003
60724*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.016	0.004	0.004
60726*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
60728*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
60729*	England	2017/18	W	W	11	ST-11 complex	Blood	0.25	0.004	0.004	0.004
60730*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
60731*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.002
60736*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.004
60746*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.002
60750*	England	2017/18	W	W	11	ST-11 complex	Blood	0.38	0.012	0.004	0.006
60753*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.003
60754*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.008	0.003
60756*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.003
60762*	England	2017/18	W	W	10651	ST-11 complex	Blood	0.094	0.023	0.006	0.006
60763*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.003
60765*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.003
60769*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.003
60770*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.003
60773*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
60776*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
60778*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.004
60784*	England	2017/18	W	W	11	ST-11 complex	Blood	0.25	0.016	0.003	0.003
60786*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.023	0.004	0.004
60791*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.023	0.003	0.002
60792*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.008	0.004	0.002
60795*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.023	0.004	0.003
60796*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.008	0.003
60797*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
60801*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.023	0.004	0.003
60802*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.004
60803*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002

60805*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.008	0.003
60808*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.003	0.004	0.003
60825*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.004
60830*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.004
60833*	England	2017/18	W	W	13720	ST-11 complex	Blood	0.064	0.023	0.008	0.004
60837*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.004
60844*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.016	0.006	0.004
60850*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.003
60853*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.008	0.003
60867*	England	2016/17	W	W	12511	ST-11 complex	Blood	0.047	0.012	0.008	0.003
60876*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.008	0.002
60877*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
60880*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.008	0.006	0.003
60883*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.016	0.006	0.004
60884*	England	2017/18	W	W	11	ST-11 complex	Blood	0.094	0.008	0.008	0.003
60889*	England	2017/18	W	W	10651	ST-11 complex	Blood	0.125	0.016	0.004	0.006
60893*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
60895*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
60898*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.012	0.004	0.002
60905*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.003	0.004	0.003
60906*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
60907*	England	2016/17	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.003
60919*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.016	0.008	0.004
60922*	England	2017/18	W	W	10651	ST-11 complex	Blood	0.094	0.012	0.008	0.004
60923*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
60925*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.002	0.004	0.003
60927*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.004	0.008	0.003
60928*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
60929*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.003	0.003	0.002
60934*	England	2017/18	W	W	11	ST-11 complex	CSF	0.064	0.006	0.004	0.003
60939*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.032	0.004	0.004
60941*	England	2017/18	W	W	10651	ST-11 complex	Joint	0.064	0.008	0.006	0.003
60947*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.004
60949*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.008	0.008	0.004
60954*	England	2017/18	W	W	11	ST-11 complex	CSF	0.064	0.012	0.008	0.004
60956*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
60957*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.016	0.004	0.003
60963*	England	2017/18	W	W	11	ST-11 complex	Blood	0.094	0.006	0.004	0.004
60965*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.003
60987*	England	2016/17	W	W	11	ST-11 complex	Blood	0.047	0.016	0.008	0.003
60990*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.008	0.004	0.003
60994*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.008	0.003
60997*	England	2016/17	W	W	13729	ST-11 complex	Blood	0.047	0.008	0.004	0.004
61000*	England	2017/18	W	W	11	ST-11 complex	Blood	0.094	0.023	0.006	0.006
61002*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.003
61003*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.002
61004*	England	2017/18	W	W	10651	ST-11 complex	CSF	0.094	0.008	0.004	0.004
61008*	England	2017/18	W	W	10651	ST-11 complex	Blood	0.064	0.016	0.004	0.003
61020*	England	2016/17	W	W	11	ST-11 complex	Blood	0.19	0.006	0.004	0.004
61031*	England	2017/18	W	W	3419	ST-11 complex	CSF	0.064	0.012	0.004	0.004
61035*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.004	0.006	0.002
61037*	England	2016/17	W	W	11	ST-11 complex	Blood	0.064	0.008	0.008	0.004
61038*	England	2016/17	W	W	11	ST-11 complex	Blood	0.38	0.012	0.004	0.004
61569*	England	2017/18	W	W	11	ST-11 complex	Blood	0.19	0.008	0.004	0.004
61570*	England	2017/18	W	W	13920	ST-11 complex	Blood	0.38	0.016	0.004	0.016
61571*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
61572*	England	2017/18	W	W	11	ST-11 complex	Blood	0.19	0.004	0.006	0.003
63561*	England	2018/19	NG	W	11	ST-11 complex	Blood	0.047	0.023	0.002	0.002
63564*	England	2017/18	W	W	11	ST-11 complex	Blood	0.094	0.012	0.006	0.004
63565*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
63566*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.003
63568*	England	2018/19	W	W	11	ST-11 complex	Blood	0.094	0.008	0.004	0.003
63569*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.002
63570*	England	2018/19	W	W	11	ST-11 complex	Joint	0.047	0.006	0.004	0.003
63571*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.012	0.003	0.004
63572*	England	2018/19	W	W	11	ST-11 complex	Blood	0.032	0.008	0.004	0.006
63574*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
63575*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.094	0.004	0.002
63577*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.003
63578*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.003
63580*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.004	0.004	0.002
63581*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
63582*	England	2018/19	W	NK	11	ST-11 complex	Blood	0.047	0.004	0.004	0.003
63583*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.006
63586*	England	2016/17	W	W	11	ST-11 complex	Joint	0.064	0.008	0.008	0.004
63587*	England	2017/18	W	W	11	ST-11 complex	Blood	0.38	0.016	0.004	0.006
63588*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.004	0.003	0.002
63589*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.003	0.004	0.003
63592*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.016	0.004	0.002
63593*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.004	0.004	0.003
63594*	England	2018/19	W	W	10651	ST-11 complex	Blood	0.064	0.012	0.004	0.004
63597*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.016	0.004	<0.002
63598*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.004
63599*	England	2017/18	W	W	11	ST-11 complex	Blood	0.38	0.012	0.004	0.004
63600*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002

63601*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.008	0.006	0.003
63603*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.003
63604*	England	2018/19	W	W	11	ST-11 complex	Blood	0.032	0.003	0.006	0.002
63606*	England	2018/19	W	NK	11	ST-11 complex	Blood	0.047	0.016	0.004	0.002
63607*	England	2018/19	W	W	11	ST-11 complex	Joint	0.064	0.047	0.008	0.003
63608*	England	2018/19	W	W	11	ST-11 complex	Blood	0.023	0.003	0.004	<0.002
63609*	England	2018/19	W	W	11	ST-11 complex	Blood	0.25	0.032	0.006	0.006
63610*	England	2018/19	W	W	11	ST-11 complex	Blood	0.023	0.004	0.004	<0.002
63611*	England	2018/19	W	NK	15541	ST-11 complex	Joint	0.047	0.016	0.008	0.003
63612*	England	2018/19	W	W	11	ST-11 complex	Blood Culture	0.064	0.008	0.006	0.002
63614*	England	2018/19	W	W	11	ST-11 complex	Joint	0.064	0.004	0.008	0.003
63615*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.023	0.004	0.004
63616*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.047	0.006	0.003
63617*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.006	0.008	0.003
63618*	England	2018/19	W	W	4977	ST-11 complex	Blood	0.25	0.012	0.004	0.004
63619*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.016	0.004	0.003
63620*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.032	0.008	0.004
63621*	England	2018/19	W	W	4977	ST-11 complex	Blood	0.25	0.016	0.008	0.008
63622*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.19	0.008	0.003
63623*	England	2018/19	W	W	11	ST-11 complex	Blood	0.25	0.012	0.006	0.006
63624*	England	2018/19	W	NK	11	ST-11 complex	Blood	0.064	0.006	0.008	0.003
63625*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.012	0.008	0.004
63628*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.012	0.008	0.003
63629*	England	2018/19	W	NK	11	ST-11 complex	Joint	0.094	0.016	0.004	0.003
63630*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
63631*	England	2018/19	W	NK	11	ST-11 complex	Blood	0.047	0.006	0.006	0.002
63632*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.016	0.004	0.004
70990*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.006	0.004	0.003
70995*	England	2017/18	W	W	11	ST-11 complex	Blood	0.023	0.008	0.004	<0.002
70996*	England	2017/18	W	W	11	ST-11 complex	Blood Culture	0.047	0.008	0.006	0.004
70997*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.006	0.003
70998*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.004
71000*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
71002*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.003
71003*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.125	0.004	0.006
71006*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
71009*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.012	0.004	0.003
71012*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
71030*	England	2017/18	W	W	10651	ST-11 complex	Blood	0.064	0.012	0.008	0.004
71031*	England	2017/18	W	W	11	ST-11 complex	Blood	0.023	0.008	0.004	0.002
71032*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
71033*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.012	0.004	0.003
71037*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.016	0.004	0.002
71043*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.008	0.003	0.004
71045*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.003
71046*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.004
71051*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.012	0.003	0.002
71052*	England	2017/18	W	W	11	ST-11 complex	Blood	0.75	0.19	0.004	0.008
71061*	England	2018/19	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
71062*	England	2018/19	W	W	11	ST-11 complex	Joint	0.19	0.003	0.006	0.003
71064*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.032	0.006	0.003
71069*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.008	0.006	0.004
71071*	England	2018/19	W	W	11	ST-11 complex	Blood	0.19	0.006	0.004	0.003
71075*	England	2018/19	W	NK	11	ST-11 complex	Blood	0.032	0.006	0.006	0.003
71080*	England	2018/19	W	W	3419	ST-11 complex	Blood	0.094	0.008	0.006	0.004
71088*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.012	0.006	0.002
71089*	England	2018/19	W	W	11	ST-11 complex	Blood	0.25	0.008	0.004	0.004
71099*	England	2018/19	W	W	11	ST-11 complex	Blood	0.094	0.008	0.008	0.004
71102*	England	2018/19	W	W	11	ST-11 complex	Joint	0.047	0.006	0.006	0.002
71106*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.032	0.006	0.002
71107*	England	2018/19	W	W	11	ST-11 complex	CSF	0.047	0.004	0.004	0.002
71113*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.006	0.006	0.003
71115*	England	2018/19	W	W	11	ST-11 complex	Blood	0.094	0.016	0.006	0.004
71121*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.006	0.008	0.003
71124*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.008	0.006	0.003
71126*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
71135*	England	2018/19	W	W	10651	ST-11 complex	Blood	0.047	0.016	0.004	0.004
71136*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.003	0.004	0.003
71137*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.003	0.004	0.003
71142*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.003
71148*	England	2018/19	W	W	11	ST-11 complex	Blood	0.25	0.004	0.004	0.004
71151*	England	2018/19	W	W	11	ST-11 complex	Blood	0.032	0.004	0.006	0.003
71152*	England	2018/19	W	W	11	ST-11 complex	Blood	0.19	0.004	0.004	0.006
71153*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.003	0.006	0.004
71159*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.003
71160*	England	2018/19	W	W	11	ST-11 complex	Blood	0.094	0.032	0.006	0.006
71162*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.003	0.004	0.003
71170*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.006	0.006	0.002
85527*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.012	0.006	0.003
85532*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.012	0.004	0.003
85535*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.006	0.003
85538*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.032	0.004	0.003
85540*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.008	0.006	0.004
85543*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.047	0.004	0.003
85546*	England	2017/18	W	W	11	ST-11 complex	Joint	0.5	0.016	0.006	0.008

85552*	England	2017/18	W	W	11	ST-11 complex	CSF	0.047	0.006	0.004	0.003
85556*	England	2017/18	W	W	11	ST-11 complex	Blood	0.19	0.004	0.004	0.006
85562*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
85563*	England	2017/18	W	W	1287	ST-11 complex	Blood	0.064	0.012	0.004	0.004
85569*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	0.002
85571*	England	2017/18	W	W	11	ST-11 complex	Blood	0.064	0.016	0.004	0.002
85572*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.004	0.004	0.002
85574*	England	2017/18	W	W	11	ST-11 complex	CSF	0.047	0.004	0.003	0.003
85581*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.003	0.003
85586*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
85590*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.006	0.003	<0.002
85599*	England	2018/19	W	W	11	ST-11 complex	Blood	0.38	0.032	0.004	0.006
91759*	England	2015/16	W	NK	11	ST-11 complex	Blood	0.064	0.25	0.004	0.003
91760*	England	2018/19	W	W	11	ST-11 complex	Blood	0.5	0.023	0.004	0.004
91761*	England	2018/19	W	NK	11	ST-11 complex	Blood	0.38	0.012	0.004	0.004
91762*	England	2018/19	W	W	11	ST-11 complex	Blood	0.5	0.008	0.004	0.006
91763*	England	2018/19	W	W	11	ST-11 complex	Blood	0.38	0.008	0.006	0.006
91764*	England	2018/19	W	W	13920	ST-11 complex	Blood	0.38	0.023	0.006	0.016
91765*	England	2018/19	W	W	11	ST-11 complex	Blood	0.38	0.016	0.008	0.006
91766*	England	2018/19	W	W	11	ST-11 complex	Blood	0.38	0.012	0.006	0.004
94185*	England	2017/18	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	<0.002
94186*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.008	0.006	0.003
94262*	England	2017/18	W	W	11	ST-11 complex	Blood	0.19	0.004	0.004	0.008
94264*	England	2017/18	W	W	11	ST-11 complex	Blood	0.047	0.006	0.004	<0.002
94269*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.008	0.004	0.003
94272*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.004	0.004	0.004
94276*	England	2018/19	W	W	10651	ST-11 complex	Blood	0.094	0.006	0.004	0.003
94282*	England	2018/19	W	W	6881	ST-11 complex	Blood	0.064	0.006	0.004	0.003
94285*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.008	0.004	0.003
94286*	England	2018/19	W	W	11	ST-11 complex	Blood	0.032	0.006	0.004	0.002
94304*	England	2018/19	W	W	11	ST-11 complex	Blood	0.032	0.002	0.004	0.003
94394*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.012	0.006	0.003
94396*	England	2018/19	W	W	11	ST-11 complex	Blood	0.25	0.023	0.004	0.004
94397*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.006	0.006	0.003
94405*	England	2018/19	W	NK	11	ST-11 complex	Blood	0.094	0.032	0.008	0.004
94414*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.006	0.006	0.003
94416*	England	2018/19	W	W	11	ST-11 complex	Blood	0.25	0.008	0.006	0.004
94417*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.012	0.006	0.004
94421*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.008	0.008	0.004
94448*	England	2018/19	W	W	11	ST-11 complex	Blood	0.064	0.016	0.008	0.004
94458*	England	2018/19	W	W	11	ST-11 complex	Blood	0.094	0.012	0.006	0.004
94459*	England	2018/19	W	W	11	ST-11 complex	Blood	0.094	0.016	0.006	0.003
94465*	England	2018/19	W	W	11	ST-11 complex	Blood Culture	0.125	0.016	0.008	0.004
94470*	England	2018/19	W	W	11	ST-11 complex	Blood	0.047	0.012	0.006	0.003

*=Isolate panel 3. NG = non-groupable. CNL = capsular null. UA = unassigned. NK = not known. ST = sequence type. CC = clonal complex.

Appendix 2: Isolate panel 2; Results chapter 3.2.

cc175 Sublineage	PubMLST ID	Isolate	Country	Year	Disease	ST	Clonal complex	Serogroup	*gyrA*	*penA*	*parC* (NEIS1525)
1	41526	M15 240953	England	2015	Invasive	175	ST-175 complex	NG	12	662	583
1	41727	LNP28435	France	2016	Carrier	175	ST-175 complex	NG	152	662	583
1	41896	AR03921_T0	Ethiopia	2014	Carrier	175	ST-175 complex	NG	12	662	583
1	41897	AR03921_T7	Ethiopia	2014	Carrier	175	ST-175 complex	NG	12	662	583
1	42666	AR04432_T0	Ethiopia	2014	Carrier	175	ST-175 complex	NG	12	662	583
1	42668	AR04432_T9	Ethiopia	2014	Carrier	175	ST-175 complex	NG	12	662	583
1	42784	16-180	Sweden	2016	Invasive	175	ST-175 complex	NG	187	662	583
1	47101	PT42	Italy	2016	Carrier	175	ST-175 complex	NG	152	662	583
1	47115	PT56	Italy	2016	Carrier	175	ST-175 complex	NG	152	662	583
1	49960	PL41818	England	2015	Carrier	175	ST-175 complex	NG	12	662	583
1	50082	PR40977	England	2015	Carrier	175	ST-175 complex	NG	12	662	583
1	52572	CA41519	Wales	2015	Carrier	175	ST-175 complex	NG	152	662	583
1	52614	CM41908	England	2015	Carrier	175	ST-175 complex	NG	12	662	583
1	52715	WG40897	England	2015	Carrier	175	ST-175 complex	NG	12	662	583
1	60134	AR03481	Ethiopia	2014	Carrier	175	ST-175 complex	NG	12	662	583
1	60143	AR03921	Ethiopia	2014	Carrier	175	ST-175 complex	NG	12	662	583
1	60308	AR05331	Ethiopia	2014	Carrier	175	ST-175 complex	NG	12	662	583
1	61207	AR04332	Ethiopia	2014	Carrier	175	ST-175 complex	NG	12	662	583
1	84075	2939	Italy	2017	Invasive	175	ST-175 complex	NG	12	662	583
1	84968	05-016	Norway	2018	Carrier	175	ST-175 complex	NG	12	662	583
1	85033	16-018	Norway	2018	Carrier	175	ST-175 complex	NG	12	662	583
1	88632	BT36315V1C	England	2018	Carrier	175	ST-175 complex	NG	12	662	583
1	89565	M19 240346	England	2019	Conjunctivitis	175	ST-175 complex	NG	313	662	583
1	89712	M19 240348	England	2019	Conjunctivitis	175	ST-175 complex	NG	313	662	583
1	89713	M19 240363	England	2019	Invasive	175	ST-175 complex	NG	313	662	583
1	91539	Nmiss3084	Italy	2018	Invasive	175	ST-175 complex	NG	12	662	583
1	92641	42-017	Norway	2019	Carrier	175	ST-175 complex	NG	12	662	583
1	93629	DE13567	Germany	2016	Invasive	175	ST-175 complex	NG	187	909	583
1	93630	DE13592	Germany	2016	Invasive	175	ST-175 complex	NG	187	909	583
1	93631	DE13875	Germany	2016	Invasive	175	ST-175 complex	NG	12	662	583
1	93679	DE14494	Germany	2019	Invasive	175	ST-175 complex	NG	313	662	583
2	52813	2586	Italy	2014	Invasive	5770	ST-175 complex	C	12	1	69
2	54027	M37089	Brazil	2014	NK	6525	UA	NG	12	14	14
2	54044	M37122	Brazil	2014	NK	6525	UA	NG	12	14	14
2	54058	M37152	Brazil	2014	NK	5770	ST-175 complex	NK	12	1	14
2	85387	1593673	Spain	2018	NK	5770	ST-175 complex	Y	12	220	14
3	29440	10378	South Africa	2003	NK	6218	ST-175 complex	W	12	1	14
3	34630	NM255	USA	2000	NK	2980	ST-175 complex	X	12	22	1364
3	59828	52707	South Africa	2017	Invasive	6218	ST-175 complex	Y	12	3	14
4	25822	16570	South Africa	2004	Invasive	175	ST-175 complex	Y	12	4	14
4	25823	677	South Africa	2005	Invasive	175	ST-175 complex	Y	12	4	14
4	25826	8465	South Africa	2006	Invasive	175	ST-175 complex	Y	12	4	14
4	25829	8246	South Africa	2006	Invasive	175	ST-175 complex	Y	12	4	14
4	25834	13160	South Africa	2004	Invasive	175	ST-175 complex	Y	12	4	14
4	25840	11244	South Africa	2007	Invasive	175	ST-175 complex	Y	12	4	14
4	25847	12870	South Africa	2007	Invasive	175	ST-175 complex	Y	12	4	14
4	25852	1026	South Africa	2005	Invasive	175	ST-175 complex	Y	12	4	14
4	25872	9371	South Africa	2003	Invasive	175	ST-175 complex	Y	12	4	14
4	25874	9558	South Africa	2003	Invasive	175	ST-175 complex	Y	12	4	14
4	40423	44133	South Africa	2014	Invasive	175	ST-175 complex	W/Y	12	4	14
4	40588	9634	South Africa	2003	Invasive	175	ST-175 complex	C	12	4	14
4	40593	10369	South Africa	2003	Invasive	175	ST-175 complex	C	12	4	14
4	40644	15734	South Africa	2004	Invasive	175	ST-175 complex	C	12	4	14
5	40583	9281	South Africa	2003	Invasive	8447	ST-175 complex	C	12	5	583
5	57336	AR00302	Ethiopia	2014	NK	8447	ST-175 complex	C	12	4	583
5	60403	AR07092	Ethiopia	2014	NK	8447	ST-175 complex	C	12	4	583
6	46995	M22783	Niger	2003	NK	2881	ST-175 complex	W	12	4	583
6	46997	M22804	Niger	2005	NK	2881	ST-175 complex	W	12	4	583
6	46998	M22809	Benin	2006	NK	2881	ST-175 complex	W	12	4	583
6	46999	M22811	Niger	2006	NK	2881	ST-175 complex	W	12	4	583
6	47000	M22819	Benin	2007	NK	2881	ST-175 complex	W	12	4	583
6	47001	M22822	Togo	2007	NK	2881	ST-175 complex	W	12	4	583
6	47002	M22828	Burkina Faso	2008	NK	2881	ST-175 complex	W	12	4	583
6	47004	M24705	Burkina Faso	2010	NK	8638	ST-175 complex	W	12	4	583
6	49369	2007461	Togo	2007	Invasive	2881	ST-175 complex	W	12	4	583
6	50827	LNP26952	France	2012	Invasive	2881	ST-175 complex	W	12	4	583
6	57891	15446	Spain	2002	Invasive	2881	ST-175 complex	W	12	4	583
6	57893	17106	Spain	2005	Invasive	2881	ST-175 complex	W	12	4	583
6	58241	M27619	Burkina Faso	2012	Invasive	9357	ST-175 complex	W	12	4	583
6	58291	M25431	Burkina Faso	2012	Invasive	2881	ST-175 complex	W	12	NK	1636
n/a	20118	M10 240763	England	2010	Invasive	4051	UA	B	3	1	8
n/a	21116	M11 240475	England	2011	Invasive	4051	UA	B	3	1	19
n/a	27784	M12 240644	England	2012	Invasive	4051	UA	B	3	428	265
n/a	30177	M97 252137	England	1997	Invasive	Incomplete	UA	W	12	2	5
n/a	35742	M14 240369	England	2014	Invasive	4051	UA	B	3	14	8
n/a	39413	953	England	2015	Invasive	4051	UA	B	3	14	8
n/a	85528	M18 240129	Northern Ireland	2018	Invasive	4051	UA	B	3	3	8
n/a	85969	Nm360601	China	2006	Invasive	5540	UA	C	379	4	5
n/a	93680	DE14495	Germany	2019	Invasive	Incomplete	UA	Y	12	912	5

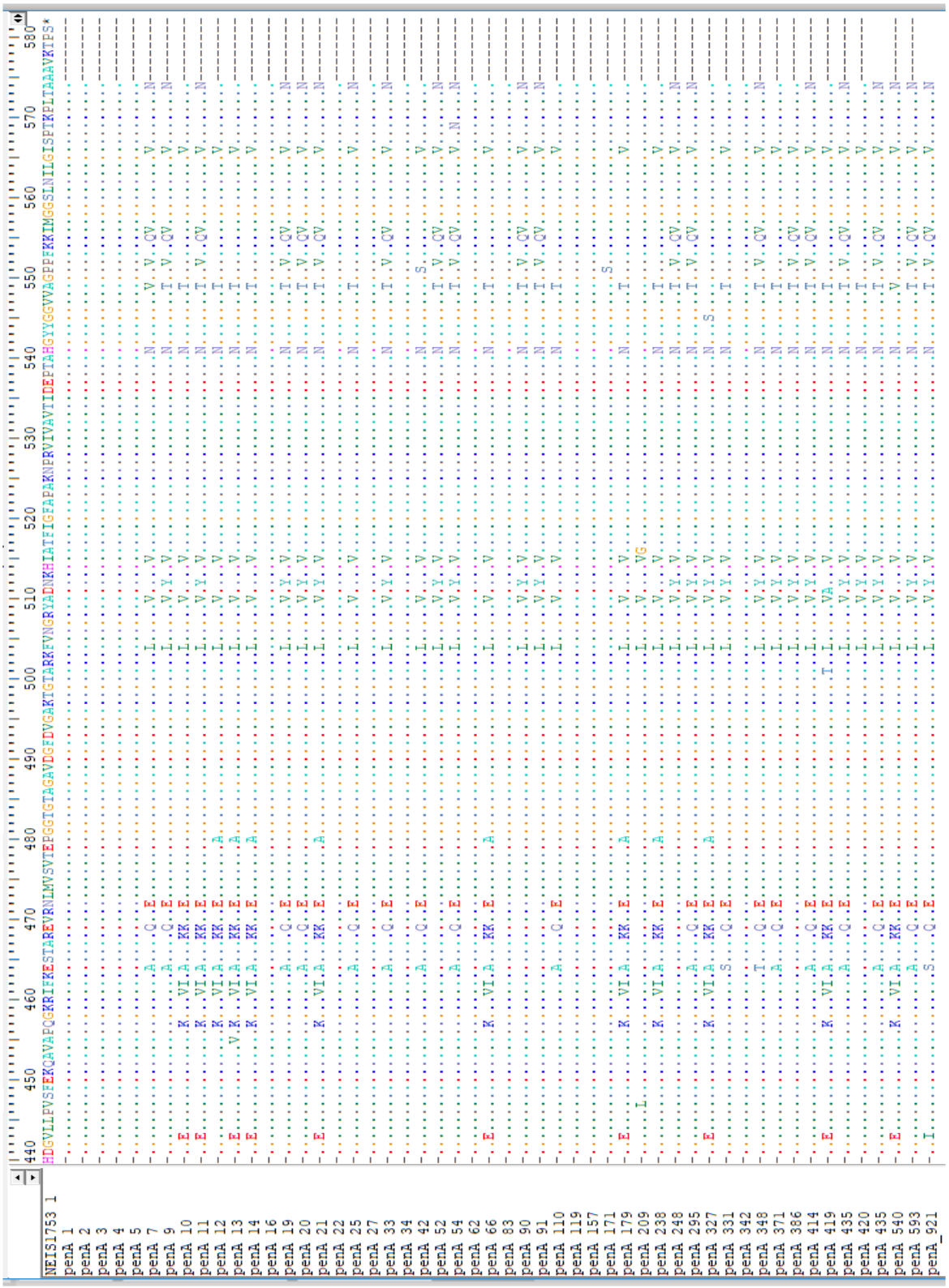
NK = not known. UA = unassigned. ST = sequence type.

Appendix 3: Isolate panel 3; Results chapter 3.3.

PubMLST ID	Year	Serogroup	Geongroup	*abcZ*	*adk*	*aroE*	*fumC*	*gdh*	*pdhC*	*pgm*	ST	CC	Penicillin MIC (mg/L)	NEIS1753 allele
20444	2011	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.064	59
38011	2015	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.064	59
42526	2016	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.064	59
47344	2016	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.047	59
72494	2017	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.047	59
72496	2017	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.064	59
60904	2017	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.094	59
60578	2018	NG	W	2	3	4	3	8	4	6	11	ST-11 complex	0.064	59
94456	2019	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.047	59
63605	2019	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.047	59
63626	2019	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.25	1086
91767	2019	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.75	253
91769	2019	W	NK	2	3	4	3	8	4	6	11	ST-11 complex	0.5	253
63590	2019	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.125	59
63584	2019	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.064	59
63585	2019	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.064	59
63591	2019	W	W	2	3	4	3	8	4	6	11	ST-11 complex	0.094	59
63567	2019	W	W	2	3	4	17	8	4	6	1287	ST-11 complex	0.094	59

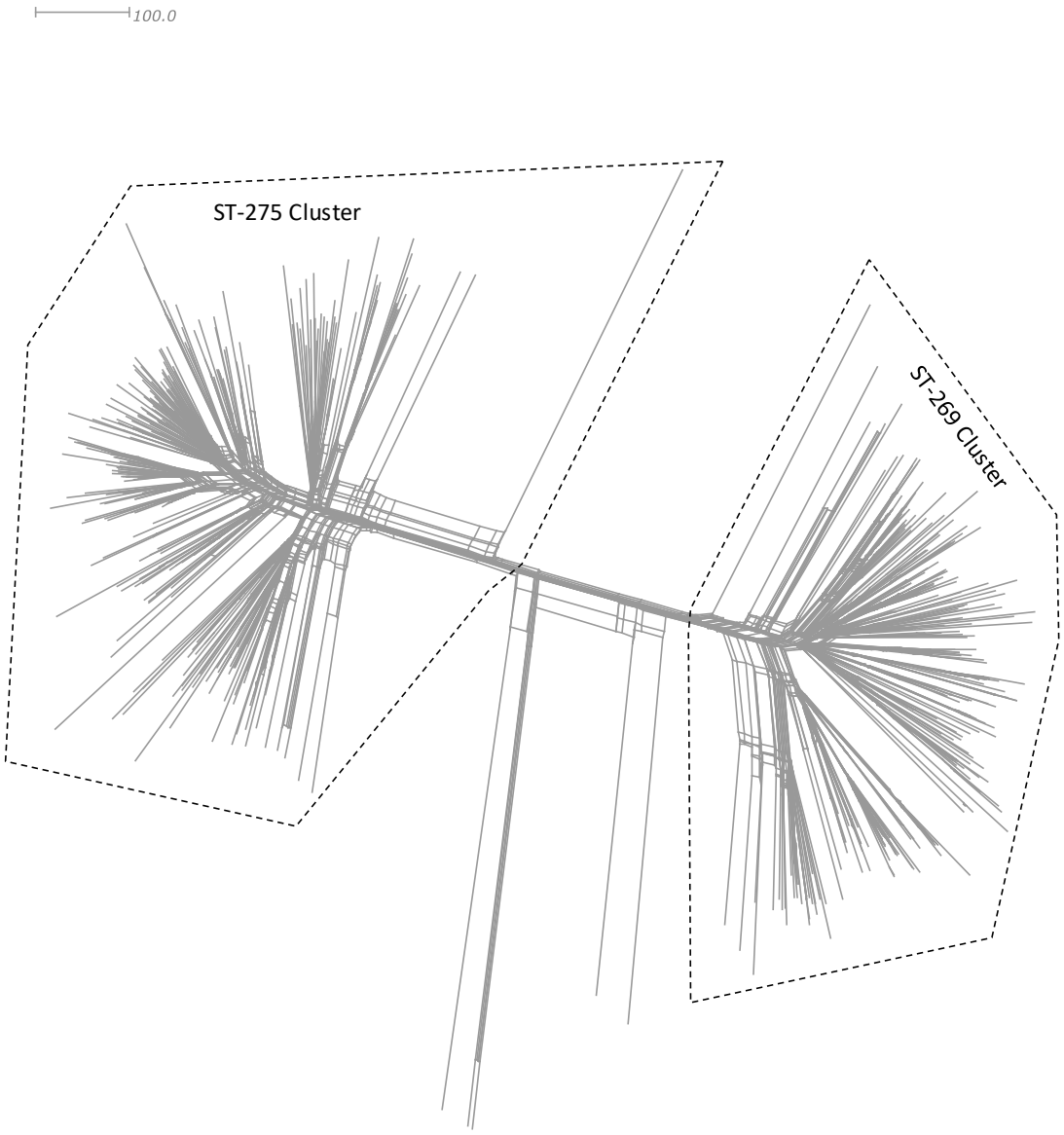
NG = non-groupable. ST = sequence type. CC = clonal complex.

Appendix 4: *PenA* alleles harboured by PenR and PenI IMD isolates in England, Wales and Northern Ireland 2010/11 – 2018/19.



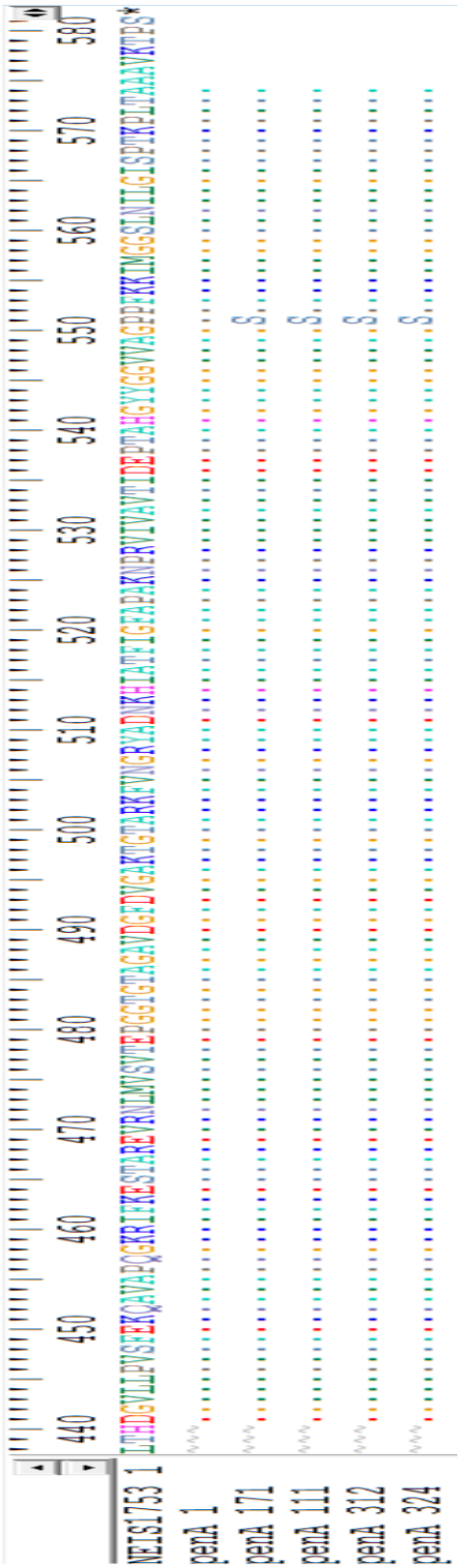
NEIS1753_1 and *penA1* = wild type alleles. The scale bar represents the amino acid position. PenR = Penicillin-resistant, PenI = Penicillin-susceptible, increased exposure according to EUCAST guidelines. *PenA* alleles among PenI isolates represented by four or more isolates.

Appendix 5: IMD isolates of ST-275 and ST-269 clusters of the ST-269 clonal complex in England, Wales and Northern Ireland 2010/11-2018/19.



Neighbor-Net phylogenetic network based on a comparison 1605 core genome loci among ST-269 clonal complex isolates (n=507). The scale bar indicates the number of different loci among the 1605 that were compared.

Appendix 6: *PenA* alleles on PubMLST with the P551S amino acid substitution.



NEIS1753_1 and *penA1* = wild type alleles. The scale bar indicates the amino acid position.

Appendix 7: Isolates on PubMLST with *penA* alleles containing the P551S amino acid substitution.

ID	Country	Year	Disease	Penicillin MIC (mg/L)	*penA* allele
9217	Czech Republic	1995	invasive (unspecified/other)	0.016	171
40556	South Africa	2005	meningitis	0.047	171
17690	Norway	2006	invasive (unspecified/other)	0.064	171
40756	South Africa	2005	meningitis	0.064	171
15674	Ireland	2008	NK	0.094	324
17121	Greece	2003	NK	0.094	111
17122	Greece	2003	NK	0.094	111
17123	Greece	2003	NK	0.094	111
17124	Greece	2003	NK	0.094	111
17125	Greece	2003	NK	0.094	111
17126	Greece	2003	NK	0.094	111
17127	Greece	2003	NK	0.094	111
28138	UK [England]	2013	invasive (unspecified/other)	0.38	171
910	UK [England]	1999	carrier	NK	171
26557	Ireland	2013	carrier	NK	324
26910	Ireland	2013	invasive (unspecified/other)	NK	324
49523	UK [Wales]	2015	carrier	NK	324
61917	Czech Republic	2018	invasive (unspecified/other)	NK	171
94513	Sweden	NK	NK	NK	324

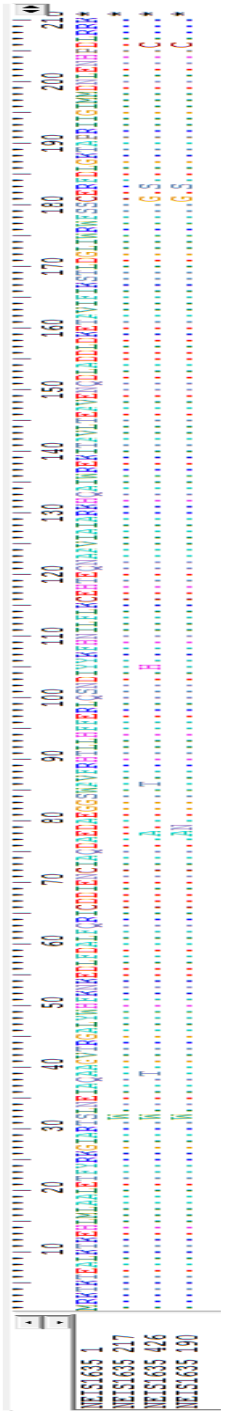
NK = not known.

Appendix 8: Variable loci between PenR isolate 28138 and two closely related PenS isolates 28132 and 28135.

Locus	Product	28132	28135	28138
NEIS0011	hypothetical protein	2	232	2
NEIS0012	hypothetical protein	70	71	70
NEIS0013	hypothetical protein	46	85	46
NEIS0071	putative lipoprotein	152	9	9
NEIS0129	30S ribosomal protein S10	1	1	15
NEIS0167	amino acid transporter	1	X	1
NEIS0213	pilin glycosyltransferase	448	X	X
NEIS0257	ribosome-associated GTPase	1	220	1
NEIS0263	hypothetical protein	1	1	X
NEIS0276	putative rotamase	357	377	357
NEIS0290	adenylosuccinate lyase	X	38	38
NEIS0338	ferric siderophore receptor protein	1	246	1
NEIS0380	O-acetyltransferase	X	509	X
NEIS0402	putative lipopolysaccharide biosynthesis translocase	48	25	25
NEIS0408	type IV secretin protein	5	1441	5
NEIS0430	hypothetical protein	1	244	1
NEIS0470	putative integral membrane protein	227	1	1
NEIS0524	putative peptidase	28	1	1
NEIS0568	glycosyltransferase	X	199	X
NEIS0586	MafB toxin	2	190	2
NEIS0599	alternative toxic C-terminal extremity	2	42	42
NEIS0638	GTP-binding protein Era	1	1	X
NEIS0651	IgA1 protease	X	37	37
NEIS0690	HPr kinase/phosphorylase	1	1	235
NEIS0717	hypothetical protein	103	2	2
NEIS0760	hypothetical protein	2	2	X
NEIS0827	type IV biogenesis protein	303	303	255
NEIS0828	type IV biogenesis protein	267	267	446
NEIS0829	type IV biogenesis protein	1155	1245	1246
NEIS0932	dihydrolipoamide succinyltransferase E2 component (EC 2.3.1.61)	250	1	1
NEIS0933	dihydrolipoamide dehydrogenase	1	251	1
NEIS0944	putative outer-membrane receptor protein	163	285	163
NEIS1002	hypothetical protein	1	1	82
NEIS1018	gamma-glutamyltranspeptidase	1	1	123
NEIS1066	putative periplasmic protein	93	5	93
NEIS1072	hypothetical protein	1	94	1
NEIS1093	sulfate adenylate transferase subunit 1	1	175	1
NEIS1099	putative GTP-binding protein	1	263	1
NEIS1103	inosine 5'-monophosphate dehydrogenase	1	269	1
NEIS1129	hypothetical protein	110	1	1
NEIS1131	putative ATP-dependent protease	1	337	1
NEIS1156	hypothetical protein	X	3	26
NEIS1170	putative P-type cation-transporting ATPase	X	1	1
NEIS1185	aspartate ammonia-lyase	1	272	1
NEIS1188	putative dnaJ-family protein	224	252	224
NEIS1296	pseudouridine synthase	1	145	1
NEIS1326	glucose-6-phosphate isomerase (EC 5.3.1.9)	1	255	1
NEIS1342	cytolysin secretion ABC transporter	1	151	1
NEIS1378	DNA mismatch repair protein	1	1	X
NEIS1442	2-C-methyl-D-erythritol 4-phosphate cytidylyltransferase	175	1	1
NEIS1447	acetate kinase	1	124	1
NEIS1504	hypothetical protein	129	1	1
NEIS1518	alanyl-tRNA synthetase	1	321	1
NEIS1526	two component sensor kinase	103	2	2
NEIS1532	hypothetical protein	1	115	1
NEIS1533	histidine-binding periplasmic protein	1	X	1
NEIS1535	potassium transporter peripheral membrane component	189	1	1
NEIS1607	DedA family integral membrane protein	1	168	1
NEIS1633	drug efflux protein	X	1	X
NEIS1635	transcriptional regulator	1	1	217
NEIS1684	aspartyl-tRNA synthetase	1	397	1
NEIS1743	cell division protein	1	134	1
NEIS1750	hypothetical protein	2	X	X
NEIS1753	penicillin-binding protein 2	59	59	332
NEIS1772	quinolinate synthetase	1	249	1
NEIS1776	beta-phosphoglucomutase	1	1	X
NEIS1777	maltose phosphorylase	351	1	1
NEIS1783	outer membrane protein class 4	2	132	2
NEIS1838	type IV biogenesis protein	2	148	2
NEIS1870	hypothetical protein	X	1	1
NEIS1879	hypothetical protein	119	1	1
NEIS1891	LysR family transcriptional regulator	1	X	1
NEIS1927	cadmium resistance protein	26	26	73
NEIS1943	outer membrane peptidase	X	186	2
NEIS1951	putative sodium-dependent inner membrane transport protein	64	165	64
NEIS1954	frataxin-like protein	133	10	10
NEIS1982	bifunctional ornithine acetyltransferase/N-acetylglutamate synthase protein	192	1	1
NEIS2021	thiamine biosynthesis protein ThiC	1	361	1
NEIS2030	putative periplasmic protein	245	1	1
NEIS2042	phosphoenolpyruvate carboxylase	1	1	377
NEIS2098	putative mafS10 cassette	1	9	1
NEIS2123	RNA polymerase sigma factor	1	1	100
NEIS2133	electron transfer flavoprotein beta-subunit	1	196	1
NEIS2138	DNA mismatch repair protein MutS	X	X	1
NEIS2141	glutamyl-tRNA synthetase	1	X	1

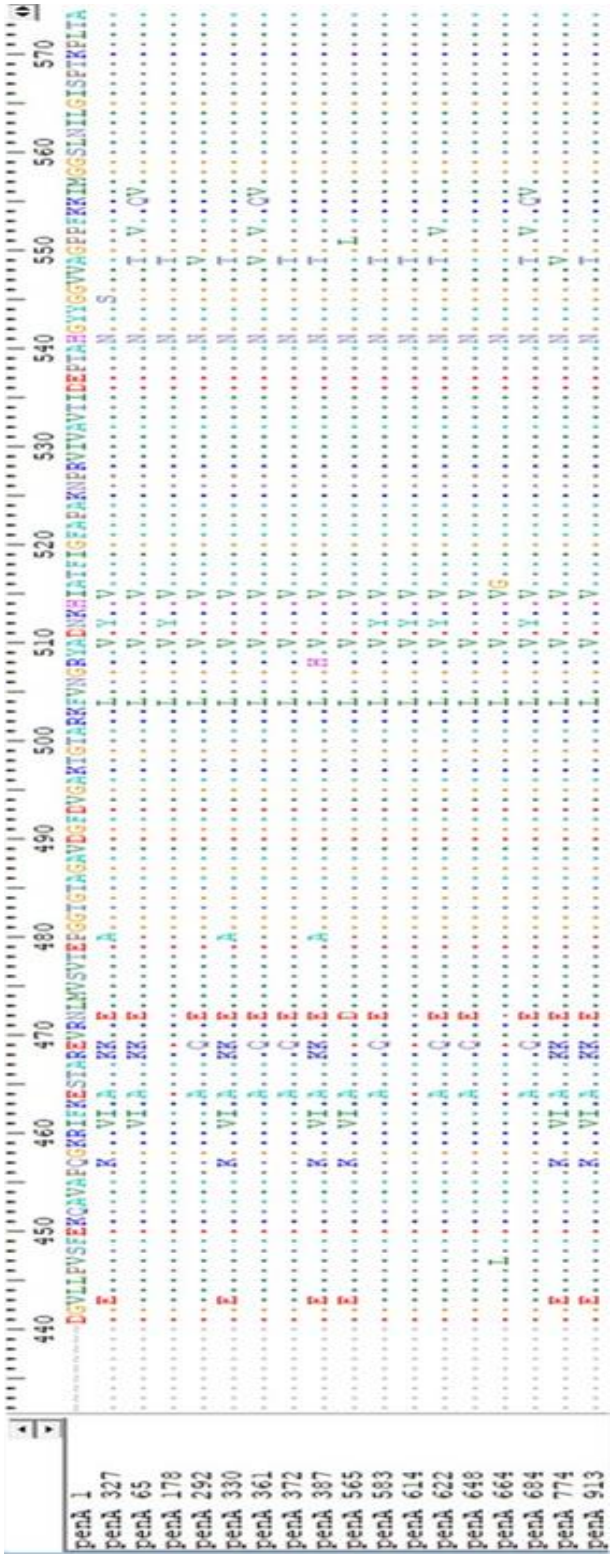
Isolates were compared on 1605 core genome loci. PenS = Penicillin-susceptible, standard exposure; PenR = Penicillin-resistant according to EUCAST guidelines. X = isolate missing complete gene.

Appendix 9: *MtrR* alleles on PubMLST containing the S32W amino acid substitution.



NEIS1635_1 = wild type *mtrR* allele. The scale bar indicates the amino acid position.

Appendix 10: *PenA* alleles on PubMLST harbouring four out of the five amino acid substitutions associated with conferring reduced susceptibility or resistance to penicillin (F504L, A510V, I515V, H541N).



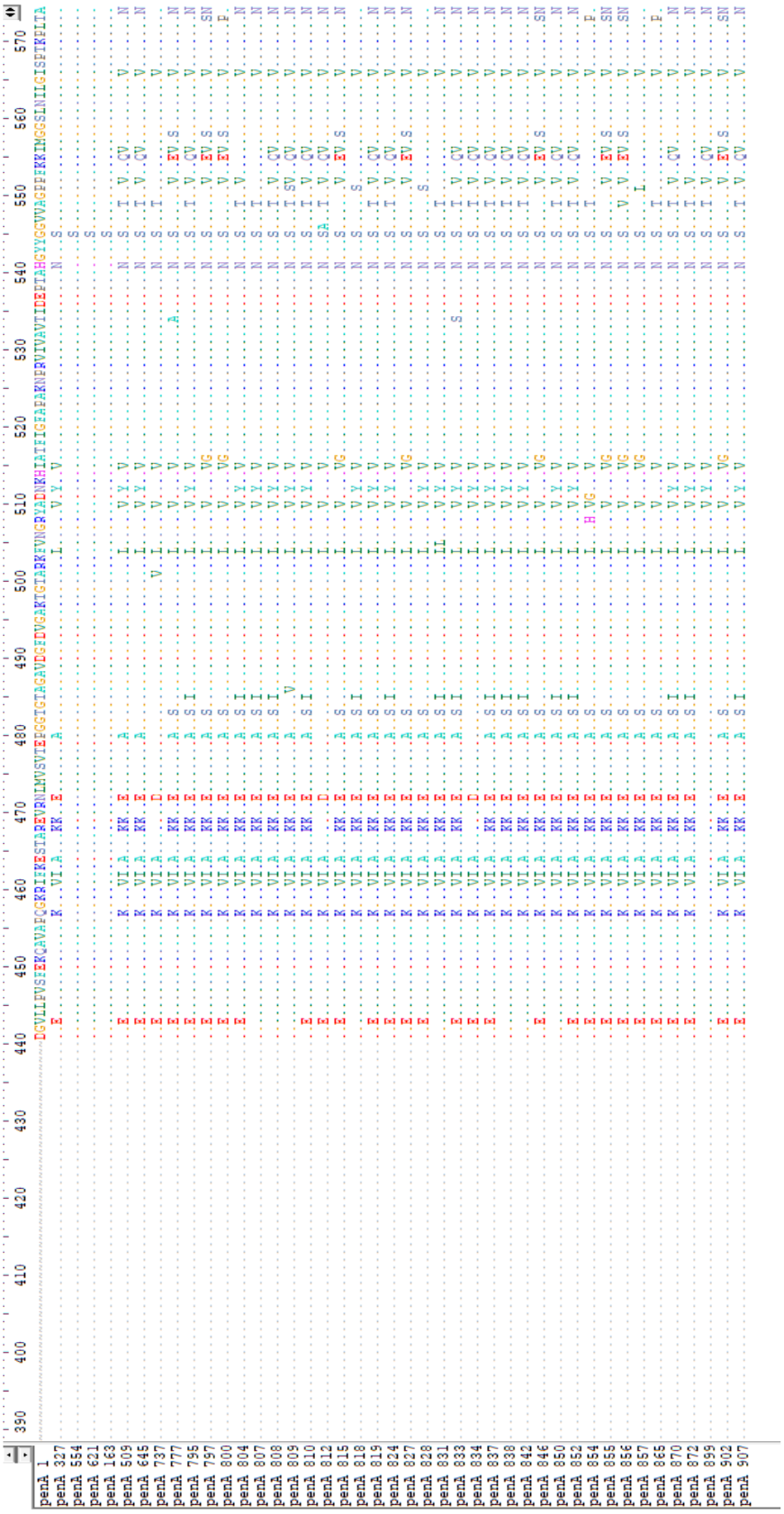
PenA1 = wild type *penA* allele. The scale bar indicates the amino acid position.

Appendix 11: Meningococcal isolates on PubMLST harbouring *penA* alleles (other than *penA327*) containing four out of the five amino acid substitutions associated with conferring reduced susceptibility or resistance to penicillin (F504L, A510V, I515V, H541N).

PubMLST ID	Country	Year	Disease	Penicillin MIC (mg/L)	*penA* allele
15176	Czech Republic	1993	invasive (unspecified/other)	0.016	622
17810	Ireland	2009	NK	0.064	292
42622	UK [Scotland]	2014	invasive (unspecified/other)	0.09	178
17689	Norway	2006	invasive (unspecified/other)	0.094	178
15778	Canada	2009	meningitis	0.094	330
15780	Canada	2009	meningitis	0.094	330
71753	New Zealand	2013	invasive (unspecified/other)	0.12	330
19389	Ireland	2012	NK	0.19	372
20716	Ireland	2012	invasive (unspecified/other)	0.25	387
35145	Australia	2014	septicaemia	0.25	565
16974	France	2005	invasive (unspecified/other)	0.38	65
18703	Ireland	2006	invasive (unspecified/other)	0.5	361
35607	UK [England]	2014	invasive (unspecified/other)	NK	648
29618	Ireland	2006	invasive (unspecified/other)	NK	361
19059	France	2012	invasive (unspecified/other)	NK	178
20727	Ireland	2012	carrier	NK	372
21025	Ireland	2012	septicaemia	NK	387
26888	Ireland	2012	invasive (unspecified/other)	NK	330
26890	Ireland	2012	invasive (unspecified/other)	NK	387
38411	Greece	2014	carrier	NK	664
40194	France	2013	NK	NK	684
41867	France	2016	invasive (unspecified/other)	NK	614
46694	UK [Scotland]	2015	carrier	NK	178
49288	Finland	2016	NK	NK	330
52814	Italy	2014	NK	NK	774
52974	Canada	2009	invasive (unspecified/other)	NK	330
53002	Canada	2009	invasive (unspecified/other)	NK	330
56674	Canada	2009	NK	NK	330
56675	Canada	2009	NK	NK	330
57541	Ireland	2006	invasive (unspecified/other)	NK	361
58168	Sweden	2017	invasive (unspecified/other)	NK	292
71580	New Zealand	2017	NK	NK	292
72823	Portugal	2019	septicaemia	NK	330
93523	Brazil	2016	carrier	NK	292

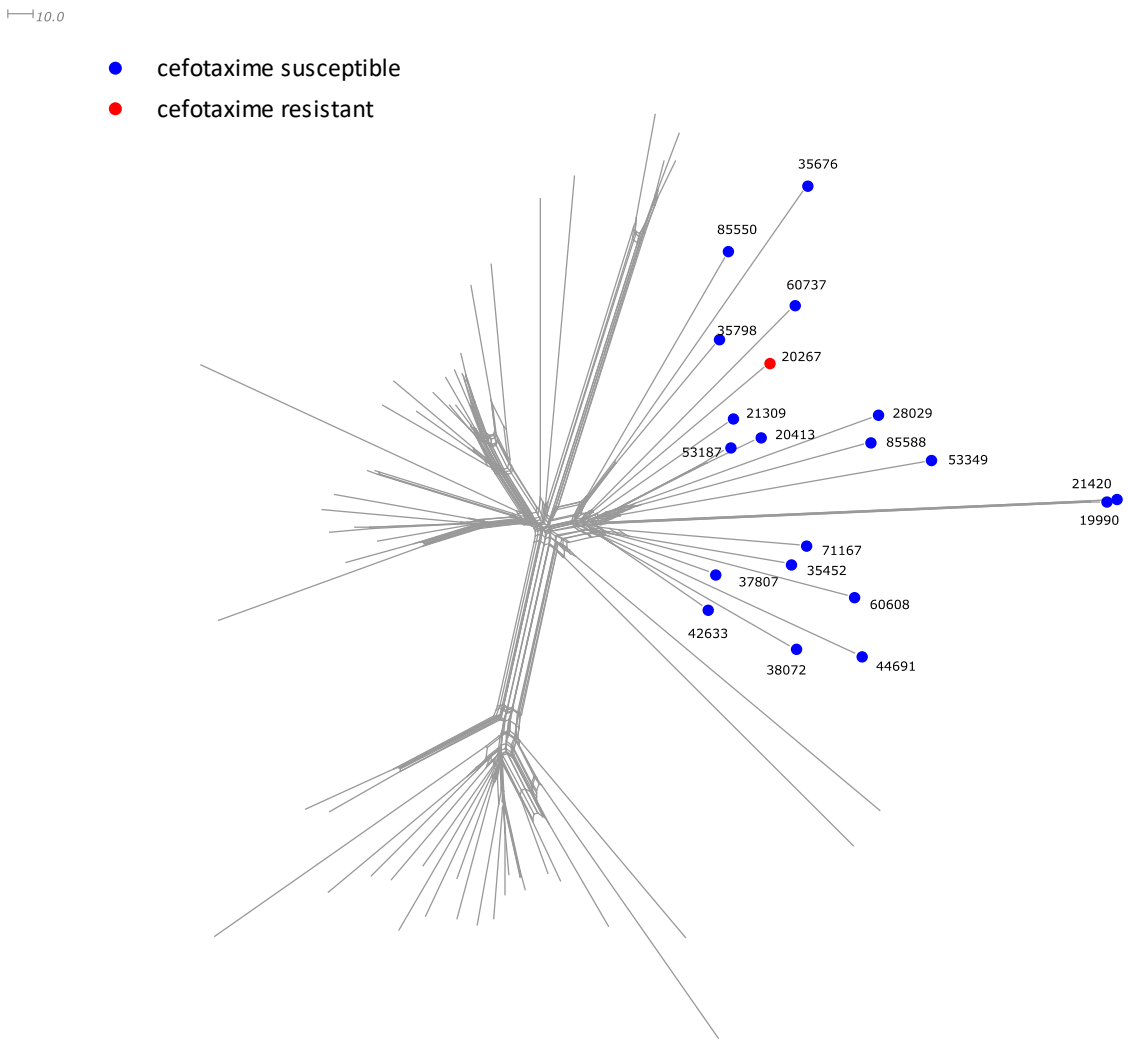
NK= not known.

Appendix 12: *PenA* alleles on PubMLST containing the G545S amino acid substitution.



PenA1 = wild type *penA* allele. The scale indicates the amino acid position.

Appendix 13: The cefotaxime-resistant ST-162 clonal complex isolate and closely related cefotaxime-susceptible ST-162 clonal complex isolates.



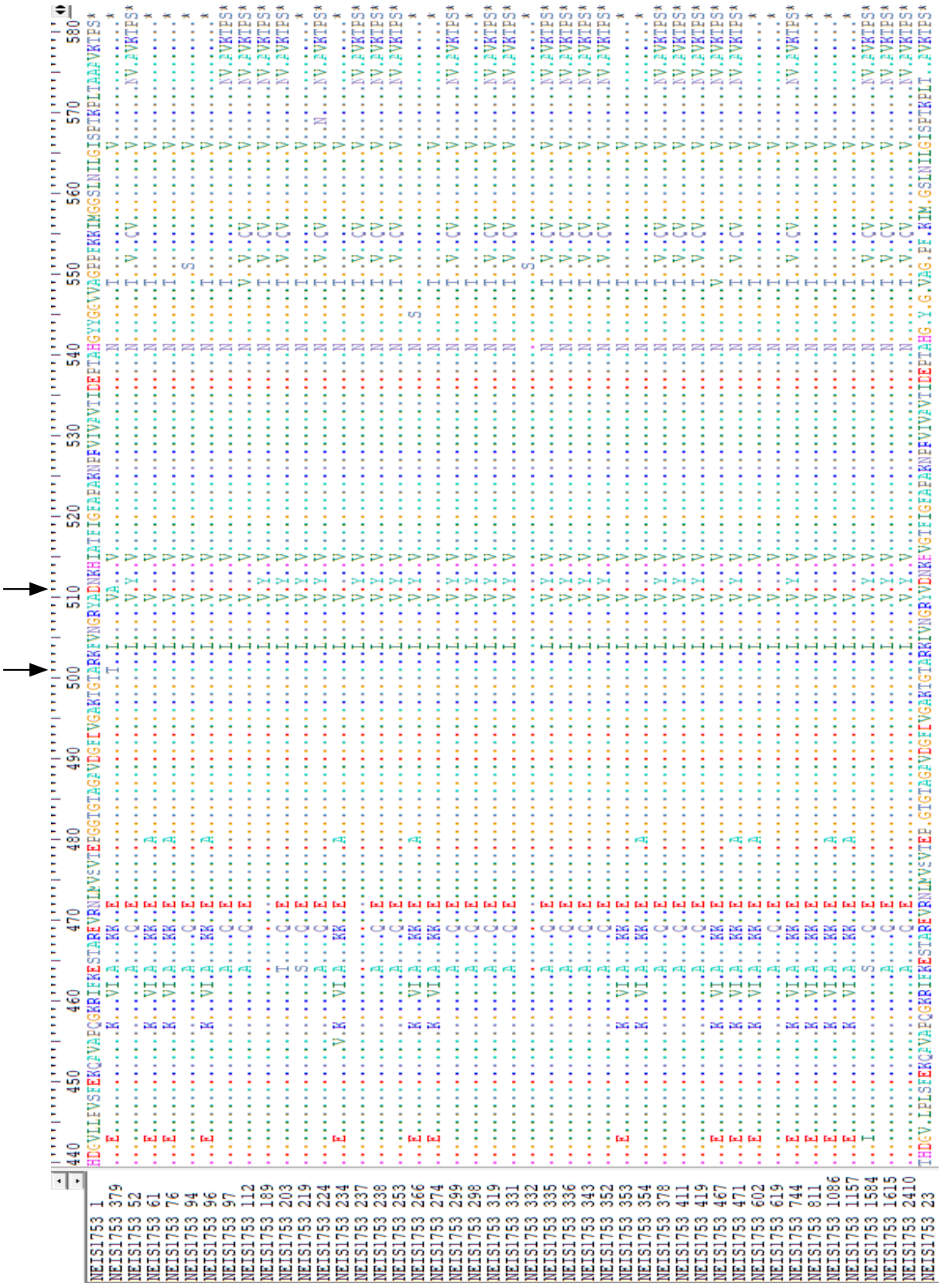
Neighbor-Net phylogenetic network based on a comparison 1605 core genome loci among PubMLST ST-162 CC isolates (n=72). The closest related cefotaxime-susceptible isolates to the cefotaxime-resistant isolate are highlighted (n=19). Isolates are labelled with PubMLST IDs. The scale bar indicates the number of different loci among the 1605 that were compared.

Appendix 14: Probable recombination events among variable loci of cefotaxime-resistant ST-162 clonal complex isolate 20267 and the closely related cefotaxime-susceptible ST-162 clonal complex isolates.

Locus	Product	20267 allele	Species Distribution
NEIS0098	aspartate carbamoyltransferase catalytic subunit	162	4 x NM
NEIS0099	pyrI	93	7 x NM
NEIS0100	hypothetical protein	3	3,180 x NM
NEIS0101	hypothetical protein	2	3, 283 x NM
NEIS0102	peptide deformylase	8	1,347 x NM
NEIS0103	methionyl-tRNA formyltransferase	9	799 x NM
NEIS0104	SUN-family protein	1	5,608 x NM
NEIS0105	hypothetical protein	1	7,983 x NM
NEIS0106	putative two-component sensor kinase	286	1 x NM
NEIS0244	NADH dehydrogenase subunit G	257	1 x NM
NEIS0245	NADH dehydrogenase I chain H	36	100 x NM
NEIS0246	NADH dehydrogenase subunit I	142	1 x NM
NEIS0247	NADH dehydrogenase I chain J	163	32 x NM
NEIS0248	NADH dehydrogenase subunit K	122	1 x NM
NEIS0709	phosphoribosylaminoimidazole-succinocarboxamide synthase	4	3,874 x NM
NEIS0710	polynucleotide phosphorylase/polyadenylase	223	1 x NM
NEIS1017	serine hydroxymethyltransferase	42	235 x NM
NEIS1018	gamma-glutamyltranspeptidase	62	1 x NM
NEIS1020	hypothetical protein	2	6, 801 x NM
NEIS1021	hypothetical protein	52	638 x NM
NEIS1022	fructose-1,6-bisphosphatase (EC 3.1.3.11)	24	545 x NM
NEIS1024	hypothetical protein	42	616 x NM
NEIS1026	putative integral membrane protein	33	1,503 x NM
NEIS1027	dihydroneopterin aldolase	85	7 x NM
NEIS1028	hypothetical protein	20	560 x NM
NEIS1029	camphor resistance protein CrcB	27	645 x NM
NEIS1030	putative integral membrane protein	33	251 x NM
NEIS1031	putative cell-division protein	102	4 x NM
NEIS1032	gamma-glutamyl phosphate reductase	136	1 x NM
NEIS1033	gamma-glutamyl kinase	19	246 x NM
NEIS1364	PorA, porin, class 1 outer membrane protein	246	5 x NM
NEIS1365	transcription elongation factor GreA	41	1,244 x NM; 2 x NG
NEIS1366	3-phosphoshikimate 1-carboxyvinyltransferase	200	1 x NM
NEIS1435	nicotinate phosphoribosyltransferase	6	491 x NM
NEIS1436	arginyl-tRNA synthetase	28	489 x NM
NEIS1552	hypothetical protein	1	520 x NM; 5 x NG
NEIS1553	Lipid A phosphoethanolamine transferase	81	8 x NM
NEIS1554	phosphoserine aminotransferase	30	123 x NM
NEIS1555	hypothetical protein	26	118 x NM
NEIS1556	transcription elongation factor NusA	52	108 x NM
NEIS1557	translation initiation factor IF-2	124	2 x NM
NEIS1558	putative integral membrane protein	101	4 x NM
NEIS1559	putative integral membrane protein	56	455 x NM
NEIS1560	hemolysin	12	503 x NM
NEIS1562	putative sodium:alanine symporter	34	465 x NM
NEIS1563	hypothetical protein	113	62 x NM
NEIS1686	putative integral membrane protein	60	11 x NM
NEIS1687	outer membrane phospholipase A precursor (ec 3.1.1.32)	44	18 x NM
NEIS1688	30S ribosomal protein S20	3	1,157 x NM; 3 x NG
NEIS1690	NK	548	1 x NM
NEIS1691	NK	592	1 x NM
NEIS1745	UDP-N-acetylmuramoyl-L-alanyl-D-glutamate synthetase	233	1 x NM
NEIS1746	hypothetical protein	220	1 x NM
NEIS1747	phospho-N-acetylmuramoyl-pentapeptide- transferase	159	1 x NM
NEIS1748	putative periplasmic protein	31	14 x NB; 2 x NM
NEIS1749	UDP-MurNAc-pentapeptide synthetase	265	1 x NM
NEIS1751	UDP-N-acetylmuramoylalanyl-D-glutamate--2, 6-diaminopimelate ligase	1616	1 x NM
NEIS1753	penicillin-binding protein 2	379	1 x NM
NEIS1754	putative small periplasmic protein	23	22 x NP; 3 x NM
NEIS1755	S-adenosyl-methyltransferase MraW	266	1 x NM
NEIS1756	cell division protein MraZ	60	4 x NB; 3 x NM
NEIS1757	hypothetical protein	98	2 x NB, 2 x NM
NEIS1759	undecaprenyl pyrophosphate phosphatase	46	59 x NB, 2 x NM

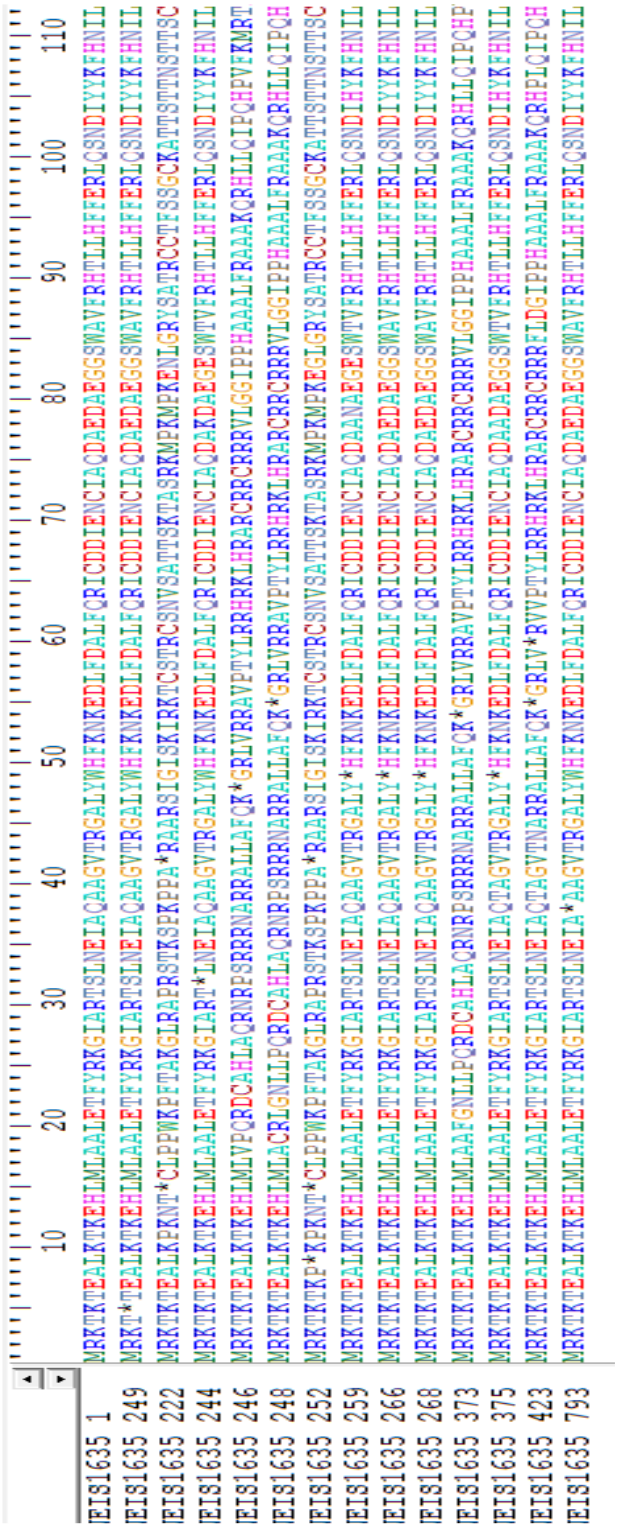
Isolates were compared in terms of all NEIS loci. PubMLST IDs of compared ST-162 clonal complex isolates can be found in Appendix 13. Species distribution refers to the number of isolates identified on PubMLST. NB = *N. Bergeri,* NG = *N. gonorrhoea*, NM = *N. meningitidis*, NP = *N. polysaccharea.*

Appendix 15: Alignment of NEIS1753 allele 379 with NEIS1753 alleles among cefotaxime-susceptible PenR IMD isolates in England, Wales and Northern Ireland, 2010/11-2018/19.



NEIS1753_1 = wild type allele. PenR = Penicillin-resistant. The scale bar indicates the amino acid position. Amino acid positions 501 and 511 are highlighted.

Appendix 16: *MtrR* alleles on PubMLST containing a frameshift within the first 60 amino acids.



NEIS1635 = wild type *mtrR* allele. * = frameshift. The scale bar indicates the amino acid position.

Appendix 17: PubMLST isolates harbouring an *mtrR* allele with a frameshift within the first 60 amino acids.

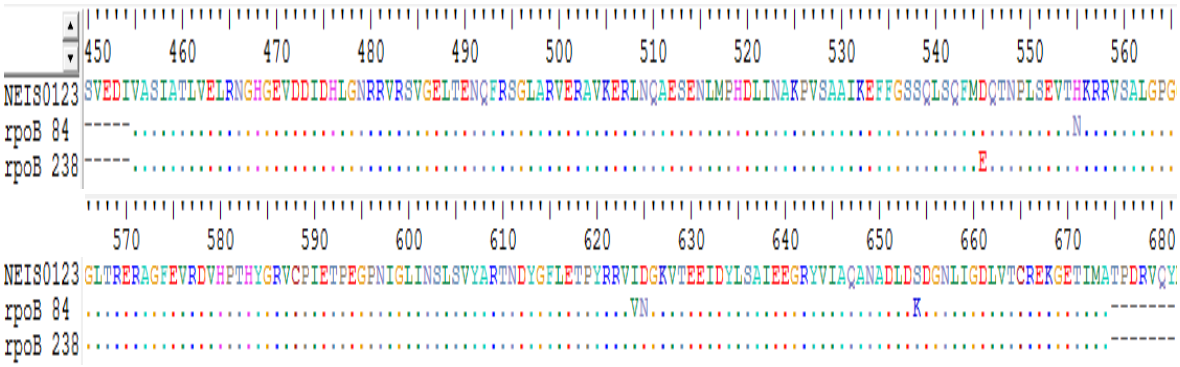
PubMLST ID	Country	Year	Species	Cefotaxime MIC (mg/L)	NEIS1635 allele
20103	UK [England]	2010	Neisseria meningitidis	0.006	244
20240	UK [Wales]	2011	Neisseria meningitidis	0.008	246
20255	UK [Wales]	2011	Neisseria meningitidis	0.006	248
20287	UK [England]	2011	Neisseria meningitidis	0.008	252
21112	UK [England]	2011	Neisseria meningitidis	0.004	259
21484	UK [England]	2012	Neisseria meningitidis	<0.002	266
26254	UK	2012	Neisseria meningitidis	NK	268
26852	Ireland	2011	Neisseria meningitidis	NK	222
57219	Czech Republic	2011	Neisseria meningitidis	NK	793
31566	USA	1999	Neisseria gonorrhoeae	NK	373
31724	India	2010	Neisseria gonorrhoeae	NK	375
34791	USA	2001	Neisseria gonorrhoeae	NK	373
36246	Kenya	2013	Neisseria gonorrhoeae	NK	423
48911	UK	NK	Neisseria gonorrhoeae	NK	373
48947	UK [England]	2004	Neisseria gonorrhoeae	NK	375
88861	USA	NK	Neisseria gonorrhoeae	NK	373

NK = not known.

Appendix 18: *RpoB* alleles among IMD isolates in England, Wales and Northern Ireland 2010/11-2018/19 and the respective rifampicin MIC values.

	Rifampicin MIC (mg/L)																			
***rpoB* allele**	**<0.002**	**0.002**	**0.003**	**0.004**	**0.006**	**0.008**	**0.012**	**0.016**	**0.023**	**0.032**	**0.047**	**0.064**	**0.094**	**0.12**	**0.125**	**0.19**	**0.25**	**0.5**	**>32**	**Total**
1				1		3	1	3	1	2	1				1					13
2		3	14	30	40	37	27	16	3	14	7	7	5		1					204
4	1	25	56	119	128	116	83	86	44	43	23	7	10		11	1	1			754
5		7	17	28	45	21	17	19	11	6	3	4	3			2				183
6		2	2	2	4	4	2	2	1			2								21
7		2	6	10	7	6	7	5	2	1	3	1								50
8			1	3	1	1	1		1						1					9
9	2	8	42	140	198	229	177	113	54	31	12	7	5	1	7	7	2			1035
18	1	14	54	105	130	134	72	39	22	24	14	14	4		3	1				631
21			1	1	2	4	3	3	3	1	1					1				20
27				2		1	1			2					1	1				8
28	1	6	13	23	39	31	27	25	16	12	2	4	2		3	1				205
31			2	6	2	5	2		1	1	1	2			1					23
33													1							1
34	7	34	127	246	138	95	55	63	24	22	13	7	2		1	1				835
38		1	1	2		1	1	3	1	2					1					13
40							1													1
42				2	4	6	5	5	1	2	1	2	1							29
44				1																1
58				1			1													2
63					1															1
69				1	2															3
70					1															1
72	1		2	4	5	3	4	1	1	2										23
73			1		3	1	1	4				1	1							12
74				1																1
75				1																1
76					1															1
77								1												1
78								1												1
80			1	1																2
81					1					1										2
82	1																			1
83					1															1
84																			1	1
85							2		1											3
86				1																1
120							2													2
144						1														1
153												1								1
162							2													2
178						1														1
210					2		1													3
216										1										1
217				1			1	1												3
218								1												1
223				1																1
224					1															1
225									1											1
226								1												1
238																		1		1
239							1													1
244						1														1
245			1																	1
246			1																	1
270					1															1
271							1													1
272							1													1
273				1																1
Total	**14**	**102**	**342**	**734**	**757**	**701**	**499**	**392**	**188**	**167**	**81**	**59**	**34**	**1**	**31**	**15**	**3**	**1**	**1**	**4122**

Appendix 19: Alignment of wild type *rpoB* gene and *rpoB* alleles found among rifampicin-resistant IMD isolates in England, Wales and Northern Ireland 2010/11-2018/19.



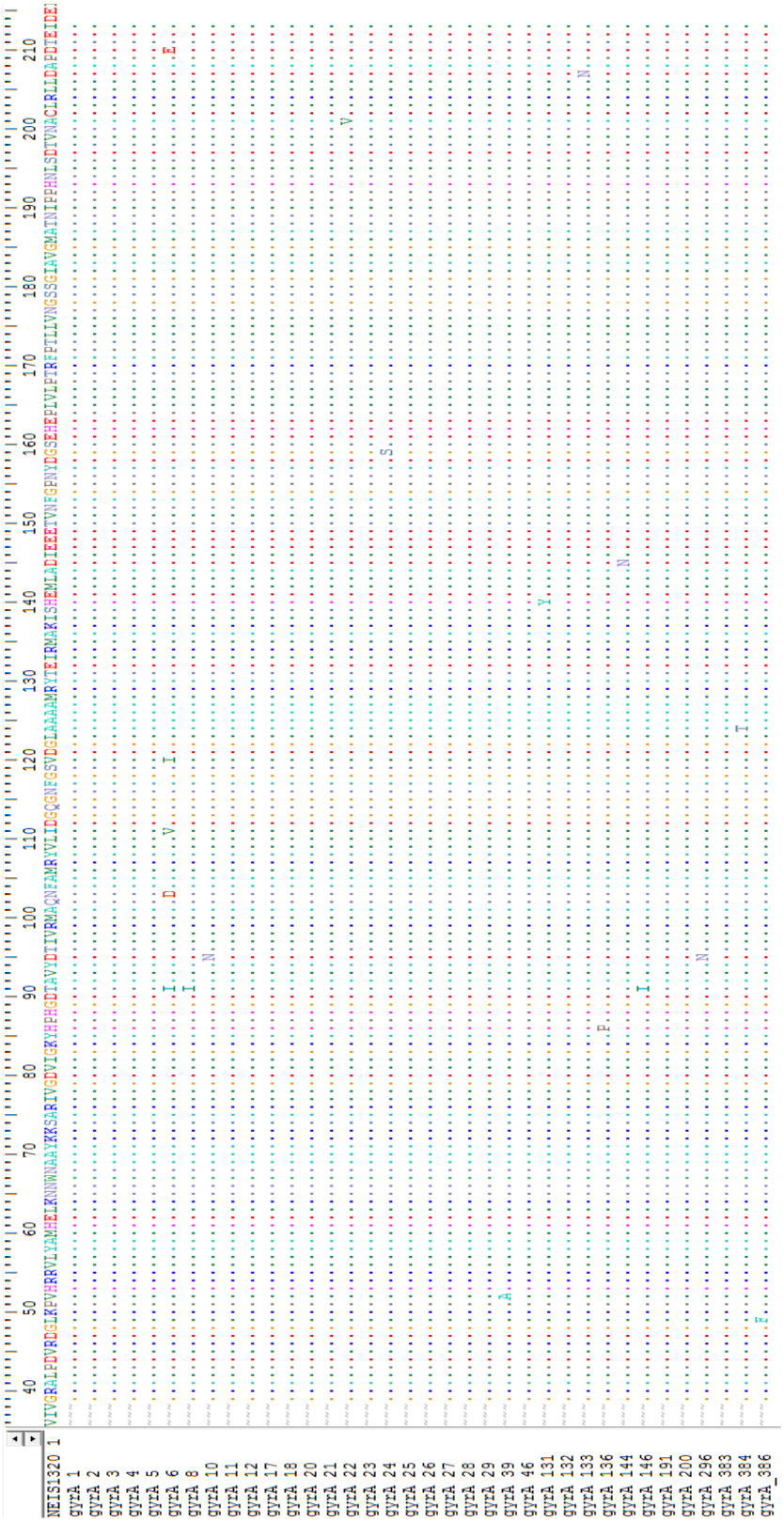
NIES0123 = full length *rpoB* gene. NEIS0123 = allele 1 = wild type *rpoB* allele. The scale bar represents the amino acid position.

Appendix 20: *GyrA* alleles harboured by IMD isolates in England, Wales and Northern Ireland 2010/11-2018/19.

***gyrA* allele**	**Number of isolates**	**MIC or MIC range (mg/L)**	***gyrA* amino acid substitutions assocaited with ciprofloxacin resistance**
1	475	<0.002-0.008	None
2	497	<0.002-0.012	None
3	354	<0.002-0.008	None
4	2,072	<0.002-0.016	None
5	19	0.002-0.006	None
6	1	**0.5***	**T91I**
8	1	**0.18***	**T91I**
10	1	**0.094***	**D95N**
11	15	0.002-0.008	None
12	626	<0.002-0.03	None
17	7	0.002-0.006	None
18	1	0.006	None
20	2	0.003-0.004	None
21	3	0.004-0.008	None
22	8	0.002-0.008	None
23	3	0.002-0.004	None
24	4	0.003-0.008	None
25	3	0.002-0.004	None
26	1	0.004	None
27	1	0.003	None
28	9	0.003-0.006	None
29	2	0.003-0.006	None
39	1	0.003	None
46	1	0.008	None
131	1	0.004	None
132	1	0.002	None
133	1	0.004	None
136	1	0.006	None
144	1	0.008	None
146	1	**0.19***	**T91I**
191	1	0.004	None
200	2	0.006-0.008	None
296	1	**0.06***	**D95N**
383	1	0.004	None
384	1	0.004	None
386	1	0.008	None
NK	2	0.004-0.008	None
Total	4122	<0.002-0.5	*

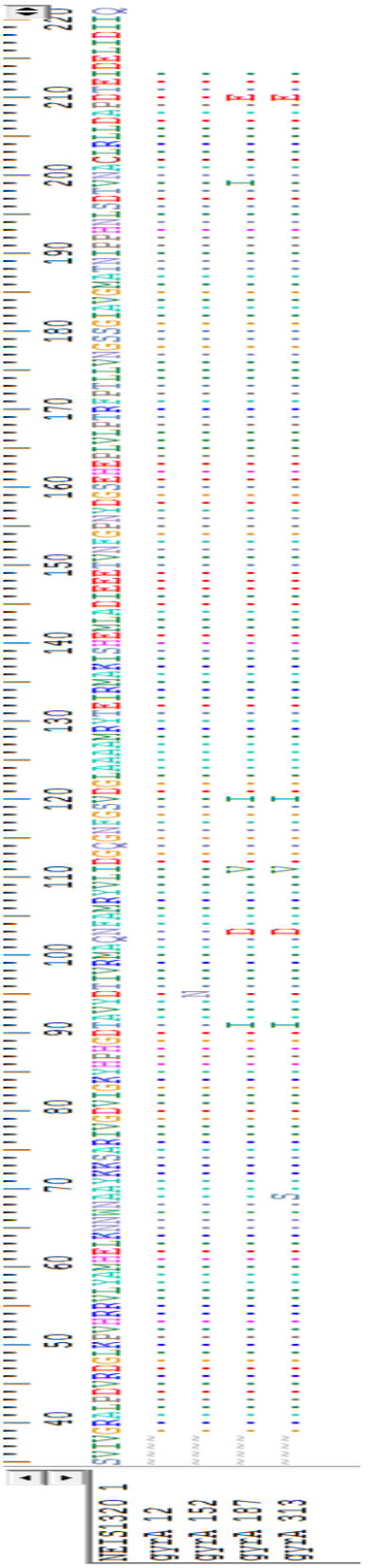
* = ciprofloxacin-resistant. NK = not known.

Appendix 21: Alignment of *gyrA* alleles harboured by IMD isolates in England, Wales and Northern Ireland 2010/11-2018/19.



NEIS1320 = full length wild type *gyrA* allele. The scale bar indicates the amino acid position.

Appendix 22: *GyrA* alleles among ST-175 clonal complex isolates.



NEIS1320 = full length wild type *gyrA* allele. The scale bar indicates the amino acid position.

Appendix 23: Serogroup W ST-11 clonal complex isolates belonging to penicillin resistance-associated lineages 1-6 (Willerton et al., 2021).

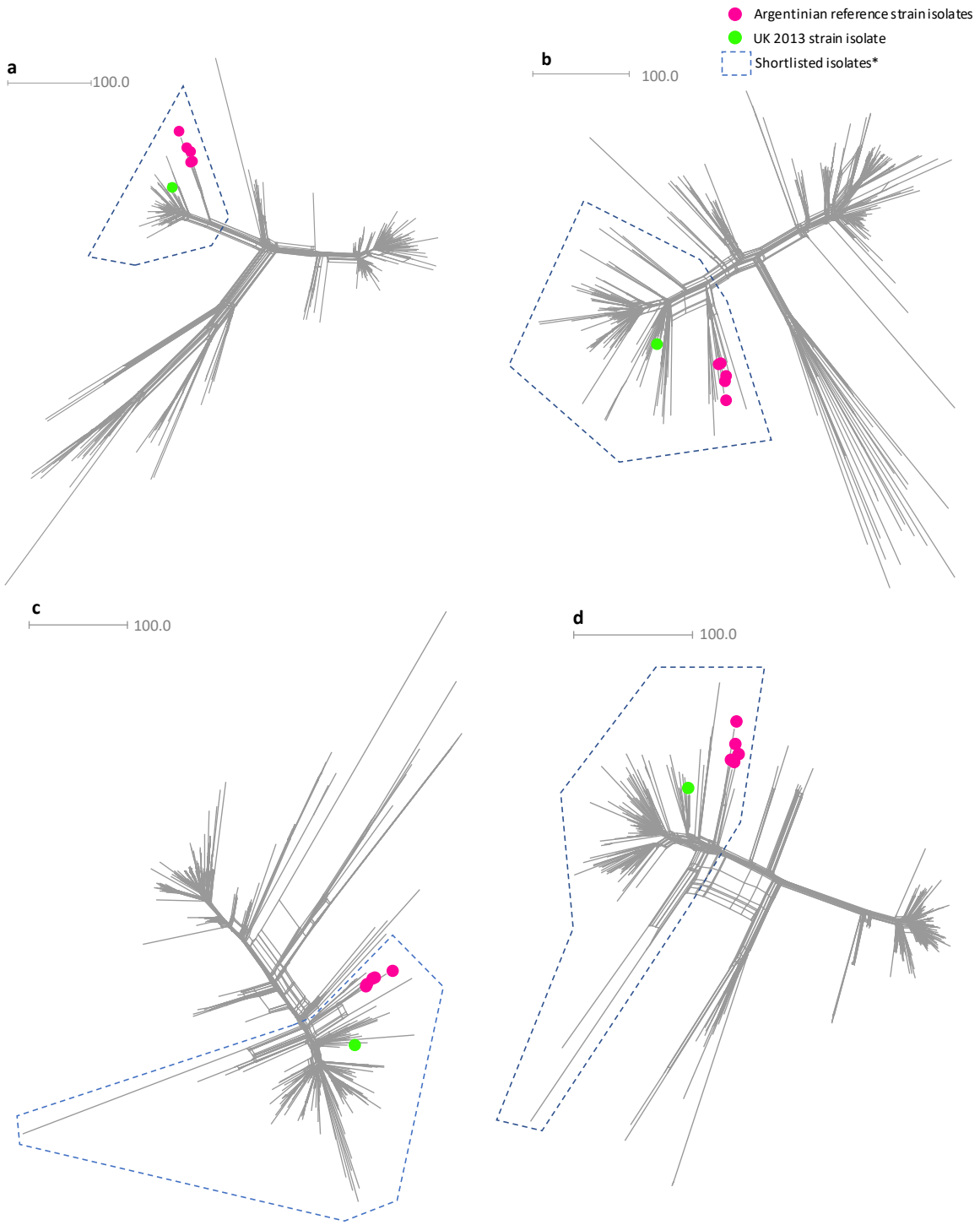
Lineage	Cluster	Strain	ID	Isolate	Country	Year	Penicillin MIC (mg/L)	*penA*
1	A	Original UK strain	53284	M17 240100	England	2017	0.032	1
1	A	Original UK strain	41501	M15 240918	England	2015	0.047	1
1	A	Original UK strain	42530	M16 240070	England	2016	0.047	1
1	A	Original UK strain	35581	M14 240090	England	2014	0.064	1
1	A	Original UK strain	47289	M16 240544	England	2016	0.064	1
1	A	Original UK strain	53067	M16 240727	England	2016	0.064	1
1	A	Original UK strain	53159	M16 240855	England	2016	0.064	1
1	A	Original UK strain	53269	M17 240073	England	2017	0.064	1
1	A	Original UK strain	60736	M17 240288	England	2017	0.064	1
1	A	Original UK strain	63577	M18 240504	England	2018	0.064	1
1	A	Original UK strain	53072	M16 240734	England	2016	0.094	1
1	A	Original UK strain	41486	M15 240896	England	2015	0.125	1
1	A	Original UK strain	26898	12002_2013	Ireland	2013	NK	1
1	A	Original UK strain	26899	12003_2013	Ireland	2013	NK	1
1	A	Original UK strain	26914	12018_2013	Ireland	2013	NK	1
1	A	Original UK strain	36131	12004_2015	Ireland	2015	NK	1
1	A	Original UK strain	93237	SMG-19-1551	Scotland	2017	NK	1
1	A	Original UK strain	83924	18-520	Sweden	2018	NK	1
1	B	Original UK strain	71591	NZ17MI0022	New Zealand	2017	0.03	9
1	B	Original UK strain	63630	M19 240302	England	2019	0.047	1
1	B	Original UK strain	61569	M18 240285	England	2018	0.19	9
1	B	Original UK strain	71558	NZ16MI0056	New Zealand	2016	0.25	9
1	B	Original UK strain	71587	NZ17MI0018	New Zealand	2017	0.25	9
1	B	Original UK strain	71621	NZ17MI0056	New Zealand	2017	0.25	9
1	B	Original UK strain	71642	NZ17MI0078	New Zealand	2017	0.25	9
1	B	Original UK strain	53230	M17 240029	England	2017	0.25	9
1	B	Original UK strain	71664	NZ18MI0018	New Zealand	2018	0.25	9
1	B	Original UK strain	71669	NZ18MI0023	New Zealand	2018	0.25	9
1	B	Original UK strain	71677	NZ18MI0031	New Zealand	2018	0.25	9
1	B	Original UK strain	71682	NZ18MI0037	New Zealand	2018	0.25	9
1	B	Original UK strain	71685	NZ18MI0040	New Zealand	2018	0.25	9
1	B	Original UK strain	71693	NZ18MI0050	New Zealand	2018	0.25	9
1	B	Original UK strain	71695	NZ18MI0053	New Zealand	2018	0.25	9
1	B	Original UK strain	71697	NZ18MI0055	New Zealand	2018	0.25	9
1	B	Original UK strain	71730	NZ18MI0091	New Zealand	2018	0.25	9
1	B	Original UK strain	71738	NZ19MI0001	New Zealand	2018	0.25	9
1	B	Original UK strain	71740	NZ19MI0003	New Zealand	2018	0.25	9
1	B	Original UK strain	63618	M19 240268	England	2019	0.25	9
1	B	Original UK strain	63621	M19 240281	England	2019	0.25	9
1	B	Original UK strain	42595	M16 240163	England	2016	0.38	9
1	B	Original UK strain	53119	M16 240794	England	2016	0.38	9
1	B	Original UK strain	58822	W-6665_Str	Greece	2017	0.38	9
1	B	Original UK strain	61038	M17 240289	England	2017	0.38	9
1	B	Original UK strain	60708	M17 240467	England	2017	0.38	9
1	B	Original UK strain	63587	M18 240200	England	2018	0.38	9
1	B	Original UK strain	63599	M18 240344	England	2018	0.38	9
1	B	Original UK strain	60750	M18 240004	England	2018	0.38	9
1	B	Original UK strain	60631	M18 240078	England	2018	0.38	9
1	B	Original UK strain	85599	M18 240404	England	2018	0.38	9
1	B	Original UK strain	91761	M18 240534	England	2018	0.38	9
1	B	Original UK strain	91763	M18 240612	England	2018	0.38	9
1	B	Original UK strain	71596	NZ17MI0027	New Zealand	2017	0.5	9
1	B	Original UK strain	71609	NZ17MI0041	New Zealand	2017	0.5	9
1	B	Original UK strain	71626	NZ17MI0062	New Zealand	2017	0.5	9
1	B	Original UK strain	71666	NZ18MI0020	New Zealand	2018	0.5	9
1	B	Original UK strain	71670	NZ18MI0024	New Zealand	2018	0.5	9
1	B	Original UK strain	71699	NZ18MI0057	New Zealand	2018	0.5	9
1	B	Original UK strain	71703	NZ18MI0061	New Zealand	2018	0.5	9
1	B	Original UK strain	71705	NZ18MI0064	New Zealand	2018	0.5	9
1	B	Original UK strain	71708	NZ18MI0067	New Zealand	2018	0.5	9
1	B	Original UK strain	71713	NZ18MI0073	New Zealand	2018	0.5	9
1	B	Original UK strain	71715	NZ18MI0075	New Zealand	2018	0.5	9
1	B	Original UK strain	71716	NZ18MI0076	New Zealand	2018	0.5	9
1	B	Original UK strain	71717	NZ18MI0077	New Zealand	2018	0.5	9
1	B	Original UK strain	71719	NZ18MI0079	New Zealand	2018	0.5	9
1	B	Original UK strain	71720	NZ18MI0080	New Zealand	2018	0.5	9
1	B	Original UK strain	71724	NZ18MI0084	New Zealand	2018	0.5	9
1	B	Original UK strain	71734	NZ18MI0096	New Zealand	2018	0.5	9
1	B	Original UK strain	91760	M18 240449	England	2018	0.5	9
1	B	Original UK strain	91762	M18 240582	England	2018	0.5	9
1	B	Original UK strain	91769	M19 240386	England	2019	0.5	9
1	B	Original UK strain	71052	M18 240297	England	2018	0.75	9
1	B	Original UK strain	91767	M19 240384	England	2019	0.75	9
1	B	Original UK strain	71711	NZ18MI0071	New Zealand	2018	1	9
1	B	Original UK strain	51888	NMLW080	Canada	2015	NK	9
1	B	Original UK strain	50313	2161610	The Netherlands	2016	NK	9
1	B	Original UK strain	41966	16-92	Sweden	2016	NK	9
1	B	Original UK strain	42206	LNP28508	France	2016	NK	9
1	B	Original UK strain	42409	LNP28524	France	2016	NK	9
1	B	Original UK strain	51880	NMLW110	Canada	2016	NK	9
1	B	Original UK strain	55150	2171500	The Netherlands	2017	NK	9
1	B	Original UK strain	58172	17-610	Sweden	2017	NK	9
1	B	Original UK strain	57906	22480	Spain	2017	NK	9
1	B	Original UK strain	57912	22565	Spain	2017	NK	9
1	B	Original UK strain	88953	NIID669	Japan	2017	NK	9
1	B	Original UK strain	55579	12018-17	Ireland	2017	NK	9
1	B	Original UK strain	93909	171049	Ireland	2017	NK	9
1	B	Original UK strain	56731	NLMW135	Canada	2017	NK	9
1	B	Original UK strain	57819	NMLW159	Canada	2017	NK	9
1	B	Original UK strain	59006	NML2017-159	Canada	2017	NK	9
1	B	Original UK strain	63003	NML2017-135	Canada	2017	NK	9
1	B	Original UK strain	85089	NML2018-164	Canada	2018	NK	1
1	B	Original UK strain	83998	2182164	The Netherlands	2018	NK	9
1	B	Original UK strain	71726	NZ18MI0087	New Zealand	2018	NK	9
1	B	Original UK strain	93936	181026	Ireland	2018	NK	9
1	B	Original UK strain	63006	NML2018-019	Canada	2018	NK	9
1	B	Original UK strain	63008	NML2018-030	Canada	2018	NK	9
1	B	Original UK strain	63009	NML2018-039	Canada	2018	NK	9
1	B	Original UK strain	63010	NML2018-044	Canada	2018	NK	9
1	B	Original UK strain	63020	NML2018-102	Canada	2018	NK	9
1	B	Original UK strain	63021	NML2018-103	Canada	2018	NK	9
1	B	Original UK strain	85078	NML2018-130	Canada	2018	NK	9
1	B	Original UK strain	85087	NML2018-153	Canada	2018	NK	9
1	B	Original UK strain	85088	NML2018-163	Canada	2018	NK	9
1	B	Original UK strain	85090	NML2018-168	Canada	2018	NK	9
1	B	Original UK strain	85094	NML2018-183	Canada	2018	NK	9

Appendix 23 continued

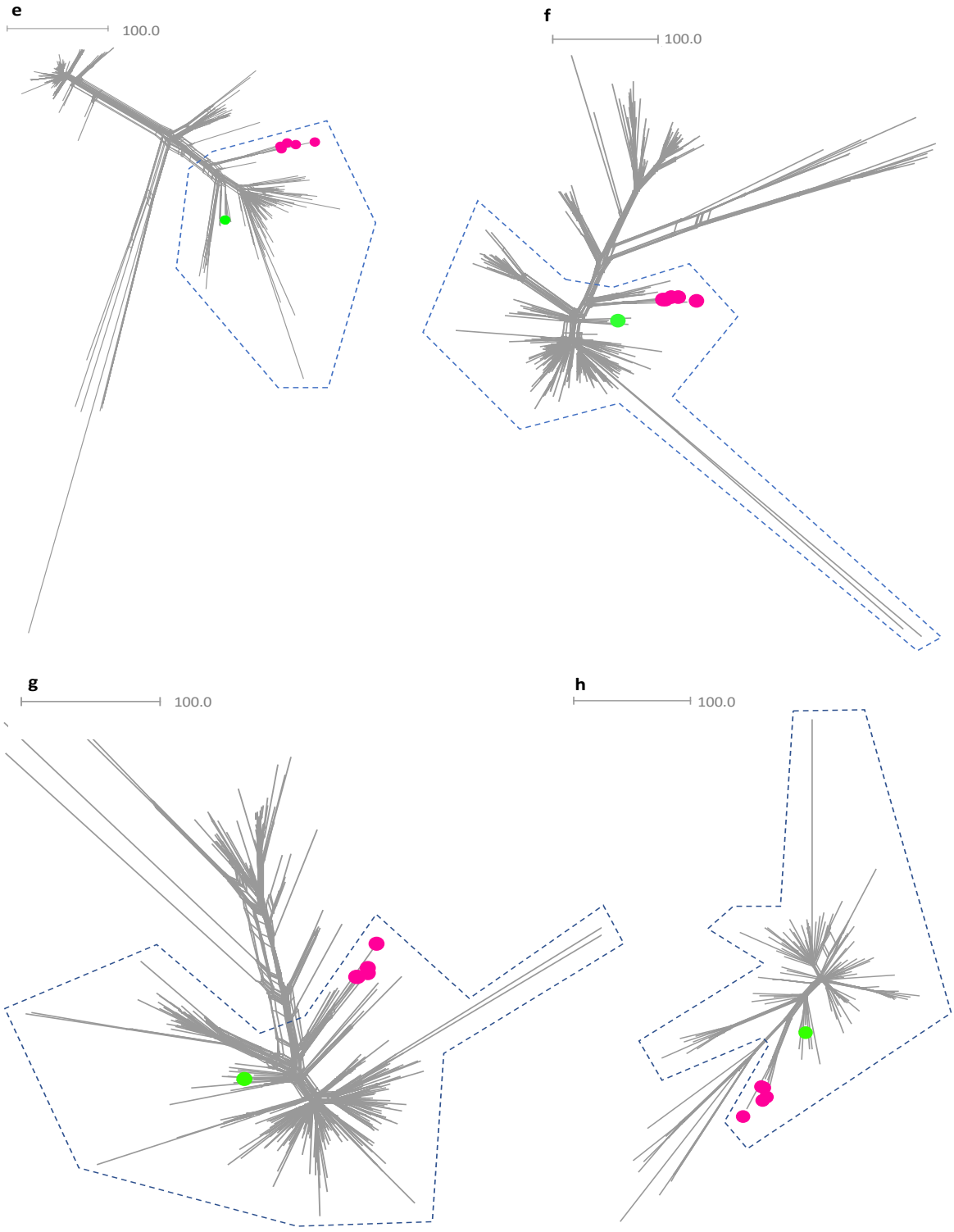
1	B	Original UK strain	85099	NML2018-192	Canada	2018	NK	9
1	B	Original UK strain	86970	2190148	The Netherlands	2019	NK	9
1	B	Original UK strain	85271	19-50	Sweden	2019	NK	9
1	B	Original UK strain	88981	19-228	Sweden	2019	NK	9
1	B	Original UK strain	63357	Nmen108	Spain	2019	NK	9
1	B	Original UK strain	63360	Nmen120	Spain	2019	NK	9
1	B	Original UK strain	63362	Nmen123	Spain	2019	NK	9
1	B	Original UK strain	91800	Nmen89	Spain	2019	NK	9
1	B	Original UK strain	93847	Nmen101	Spain	2019	NK	9
1	B	Original UK strain	93962	191001	Ireland	2019	NK	9
1	B	Original UK strain	93985	191030	Ireland	2019	NK	9
1	B	Original UK strain	71883	NML2019-158	Canada	2019	NK	9
1	B	Original UK strain	89245	NML2019-044	Canada	2019	NK	9
1	B	Original UK strain	72761	Nmen152	Spain	2020	NK	9
1	B	Original UK strain	57573	12-590-208	Sweden	NK	NK	9
1	B	Original UK strain	51212	Nmiss2913	Italy	NK	NK	9
2	A	UK 2013 strain	44820	M16_240451	Northern Ireland	2016	0.047	1
2	A	UK 2013 strain	63561	M18 240396	England	2018	0.047	1
2	A	UK 2013 strain	71159	M19 240035	England	2019	0.047	1
2	A	UK 2013 strain	47337	M16 240684	England	2016	0.064	1
2	A	UK 2013 strain	53052	M16_240706	Wales	2016	0.064	1
2	A	UK 2013 strain	53346	M17 240192	England	2017	0.064	1
2	A	UK 2013 strain	60769	M17 240488	England	2017	0.064	1
2	A	UK 2013 strain	60949	M17 240551	England	2017	0.064	1
2	A	UK 2013 strain	61031	M17 240811	England	2017	0.064	1
2	A	UK 2013 strain	72496	M17 240488b	England	2017	0.064	1
2	A	UK 2013 strain	60601	M18 240072	England	2018	0.064	1
2	A	UK 2013 strain	60663	M18 240085	England	2018	0.064	1
2	A	UK 2013 strain	63566	M18 240408	England	2018	0.064	1
2	A	UK 2013 strain	71003	M18 240189	England	2018	0.064	1
2	A	UK 2013 strain	71009	M18 240207	England	2018	0.064	1
2	A	UK 2013 strain	71043	M18 240273	England	2018	0.064	1
2	A	UK 2013 strain	85571	M18 240304	England	2018	0.064	1
2	A	UK 2013 strain	94269	M18 240420	England	2018	0.064	1
2	A	UK 2013 strain	94282	M18 240506	England	2018	0.064	1
2	A	UK 2013 strain	63595	M18 240458	Wales	2018	0.064	1
2	A	UK 2013 strain	63615	M19 240248	England	2019	0.064	1
2	A	UK 2013 strain	63632	M19 240315	England	2019	0.064	1
2	A	UK 2013 strain	63627	M19 240211	Wales	2019	0.064	1
2	A	UK 2013 strain	53084	M16 240748	England	2016	0.094	1
2	A	UK 2013 strain	63564	M18 240148	England	2018	0.094	1
2	A	UK 2013 strain	63568	M18 240444	England	2018	0.094	1
2	A	UK 2013 strain	71115	M18 240613	England	2018	0.094	1
2	A	UK 2013 strain	71080	M19 240191	England	2019	0.094	1
2	A	UK 2013 strain	94459	M19 240187	England	2019	0.094	1
2	A	UK 2013 strain	44668	2160005	The Netherlands	2016	NK	1
2	A	UK 2013 strain	57471	24170	Ireland	2017	NK	1
2	A	UK 2013 strain	57477	24176	Ireland	2017	NK	1
2	A	UK 2013 strain	63137	SMG-19-1949	Scotland	2017	NK	1
2	A	UK 2013 strain	60002	LNP29989abd	France	2018	NK	1
2	A	UK 2013 strain	84915	DE14146	Germany	2018	NK	1
2	A	UK 2013 strain	84914	DE14141	Germany	2018	NK	1
2	A	UK 2013 strain	84917	DE14193	Germany	2018	NK	1
2	A	UK 2013 strain	84916	DE14183	Germany	2018	NK	1
2	A	UK 2013 strain	84921	DE14223	Germany	2018	NK	1
2	A	UK 2013 strain	93948	181039	Ireland	2018	NK	1
2	A	UK 2013 strain	58191	SMG_18_163	Scotland	2018	NK	1
2	A	UK 2013 strain	61289	18-87	Sweden	2018	NK	1
2	A	UK 2013 strain	59769	2180800_I	The Netherlands	2018	NK	1
2	A	UK 2013 strain	59770	2180800_II	The Netherlands	2018	NK	1
2	A	UK 2013 strain	88183	DE14424	Germany	2019	NK	1
2	A	UK 2013 strain	72830	Nm_67-19	Portugal	2019	NK	1
2	A	UK 2013 strain	85392	SMG-19-325	Scotland	2019	NK	1
2	A	UK 2013 strain	88879	Nmen56	Spain	2019	NK	1
2	A	UK 2013 strain	71947	SMG-20-114	Scotland	2020	NK	1
2	B	UK 2013 strain	60784	M17 240755	England	2017	0.25	14
2	B	UK 2013 strain	71089	M18 240494	England	2018	0.25	14
2	B	UK 2013 strain	63609	M19 240309	England	2019	0.25	14
2	B	UK 2013 strain	94416	M19 240109	England	2019	0.25	14
2	B	UK 2013 strain	94396	M19 240063	England	2019	0.25	14
2	B	UK 2013 strain	63626	M19 240358	England	2019	0.25	14
2	B	UK 2013 strain	71148	M19 240018	England	2019	0.25	14
2	B	UK 2013 strain	63623	M19 240347	England	2019	0.25	14
2	B	UK 2013 strain	91765	M19 240292	England	2019	0.38	14
2	B	UK 2013 strain	91766	M19 240316	England	2019	0.38	14
2	B	UK 2013 strain	85546	M18 240166	England	2018	0.5	14
2	B	UK 2013 strain	84118	18-469	Sweden	2018	NK	14
2	B	UK 2013 strain	93335	SMG-19-1582	Scotland	2019	NK	14
3	n/a	UK 2013 strain	61570	M18 240314	England	2018	0.38	540
3	n/a	UK 2013 strain	91764	M19 240214	England	2019	0.38	540
3	n/a	UK 2013 strain	57913	22569	Spain	2017	NK	1
3	n/a	UK 2013 strain	72893	SMG-20-623	Scotland	2020	NK	1
4	n/a	Original UK strain	52889	16.8710760	Scotland	2016	0.006	1
4	n/a	Original UK strain	28128	M12 240826	England	2012	0.047	1
4	n/a	Original UK strain	39365	M15 240730	England	2015	0.047	1
4	n/a	Original UK strain	71064	M19 240144	England	2019	0.047	1
4	n/a	Original UK strain	28161	M13 240467	England	2013	0.064	1
4	n/a	Original UK strain	29734	M13 240538	England	2013	0.064	1
4	n/a	Original UK strain	39408	M15 240794	England	2015	0.064	1
4	n/a	Original UK strain	28143	M13 240158	England	2013	0.094	1
4	n/a	Original UK strain	37797	M15 240010	England	2015	0.38	9
4	n/a	Original UK strain	51883	NMLW083	Canada	2014	NK	1
4	n/a	Original UK strain	38995	15.8700107	Scotland	2015	NK	1
4	n/a	Original UK strain	39000	15.8703957	Scotland	2015	NK	1
5	n/a	Original UK strain	28117	M12 240663	England	2012	0.38	435
5	n/a	Original UK strain	26993	90149v1	UK	NK	NK	1
Singleton	n/a	Original UK strain	28138	M13 240066	England	2013	0.38	171
6	n/a	South American strain	38120	M14 240447b	England	2014	0.047	1
6	n/a	South American strain	37845	M15 240066	Wales	2015	0.125	1
6	n/a	South American strain	20057	M10 240671	England	2010	0.38	9
6	n/a	South American strain	36848	2593	Italy	2014	NK	1
6	n/a	South American strain	36779	107507	Finland	2015	NK	1
6	n/a	South American strain	36781	107497	Finland	2015	NK	1
6	n/a	South American strain	46098	LNP28711	France	2016	NK	1
6	n/a	South American strain	31319	M10208	Chile	NK	NK	1
6	n/a	South American strain	40501	M18774	USA	2009	NK	#
6	n/a	South American strain	31323	M1412	Chile	NK	NK	1

Apparent frameshift due to an extra 'A' at poly-A tract (nucleotide 1667 of NEIS1753) leading to a lengthened peptide with n=22 amino acid mismatches. Given that penicillin binding protein 2 (encoded by *penA*) is essential, this frameshift would need confirming with Sanger sequence analysis. NK= not known.

Appendix 24: Identification of non-MGL serogroup W ST-11 clonal complex isolates of the Original UK and UK 2013 strains (Willerton et al., 2021).

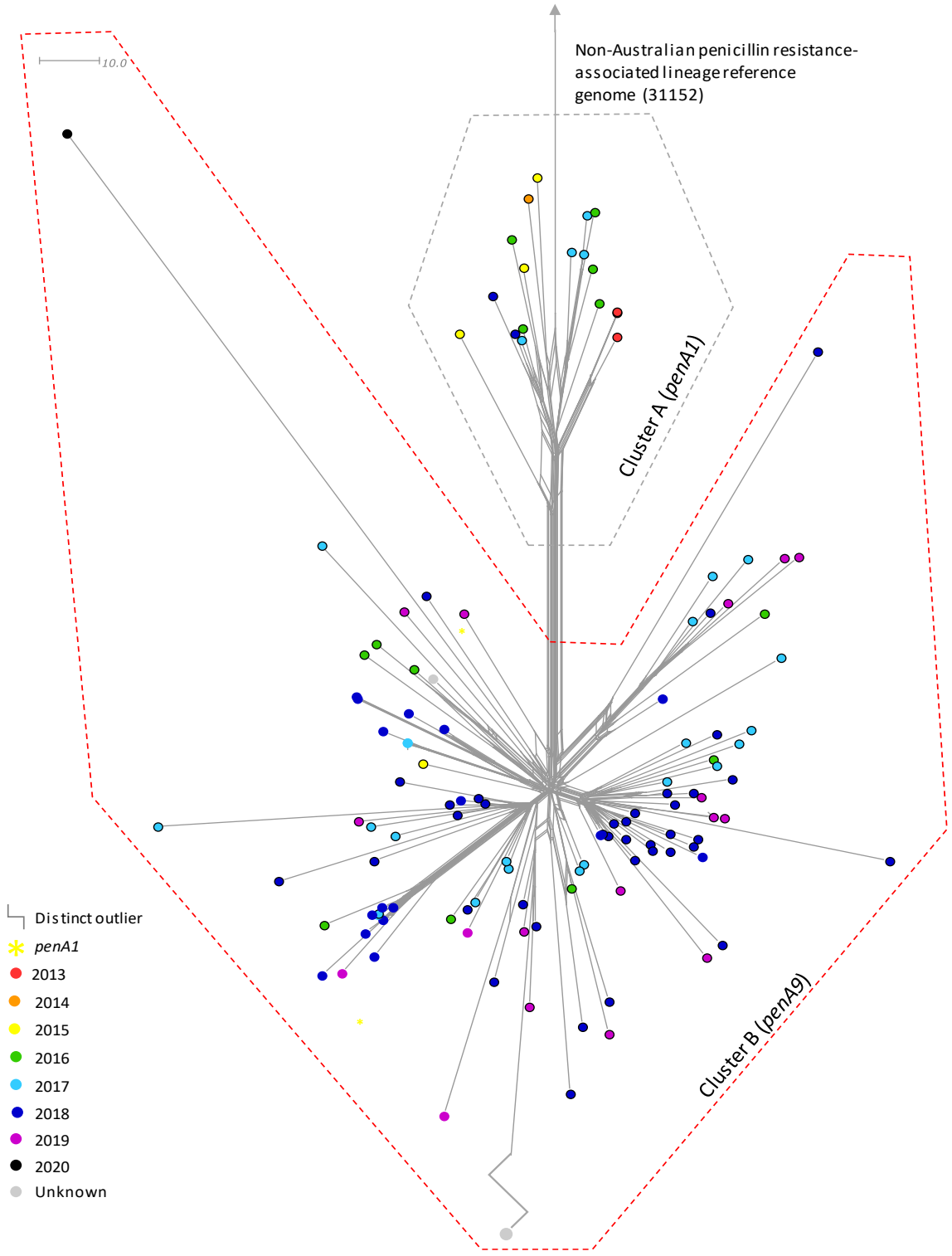


Appendix 24 Continued



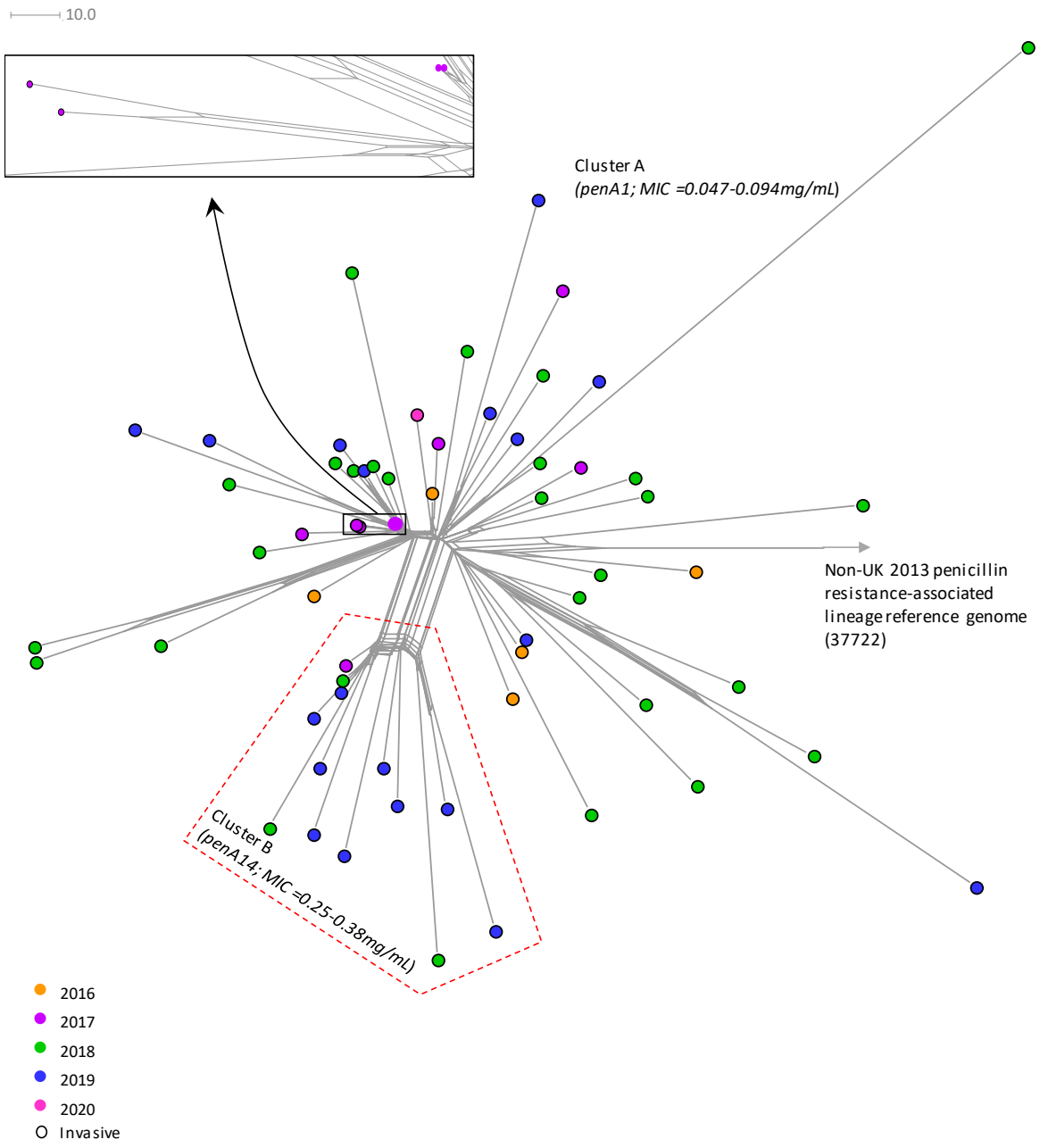
Core genome comparison based on 1605 core genome loci among non-MGL serogroup W ST-11 clonal complex isolates (n=2,214). Genomes split into eight groups (a-h). Each network includes the South American reference strain isolates (n=5; PubMLST IDs 31148, 31149, 31150, 31151, 31152) and an original UK strain reference strain (PubMLST ID 30154). The number of different loci among the 1605 compared is represented by the scale bar. *Genomes of original UK and UK 2013 strains.

Appendix 25: Serogroup W ST-11 clonal complex isolates of penicillin resistance-associated lineage 1 (Willerton et al., 2021).



Core genome comparison based on 1605 core genome loci among serogroup W ST-11 clonal complex isolates of penicillin resistance-associated lineage 1. the number of different loci among the 1605 compared is represented by the scale bar.

Appendix 26: Serogroup W ST-11 clonal complex isolates of penicillin resistance-associated lineage 2 (Willerton et al., 2021).



Core genome comparison based on 1605 core genome among serogroup W ST-11 clonal complex isolates of penicillin resistance-associated lineage 2 (n=62). The number of different loci among the 1605 compared is represented by the scale bar.